Triggering the False Suffocation Alarm in Panic Disorder Patients by Using a Voluntary Breath-Holding Procedure

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The authors compared the maximal duration of voluntary breath-holding in patients with panic disorder (N=23), patients with generalized social phobia (N=10), and healthy subjects (N=26). Patients with panic disorder had significantly shorter breath-holding durations than either comparison group. Groups did not otherwise differ in physiologic response to the breath-holding. Implications for a false suffocation alarm in panic disorder are discussed.
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Over the past decade, elucidation of the contribution of chronic hyperventilation to panic disorder has been the focus of considerable research. Several investigators have proposed that panic attacks are the direct result of chronic hyperventilation (1, 2). Conversely, others have argued that hyperventilation does not play a central role in panic disorder and is better understood as a consequence of panic sensations (3, 4) triggered by hypersensitive CO_2 receptors (5, 6).

In an attempt to integrate the existing literature on panic disorder, Klein (7) has proposed that panic is the result of an evolved, but maladaptive, suffocation alarm system that is hypersensitive to CO_2. When activated, this alarm mechanism is thought to result in respiratory distress, hyperventilation, panic, and the urge to flee. Theoretically, indicators of potential suffocation will readily provoke a sequence of respiratory events that culminate in panic. It is important to note, however, that the activation threshold of the alarm is thought to be pathologically lower in patients with panic disorder; therefore, panic is more apt to occur in situations where suffocation is not a real threat (7).

As a general test of the false suffocation alarm theory, we had subjects manipulate their respiratory pattern by holding their breath at functional residual capacity for maximum duration. This manipulation is somewhat different from that of a previous investigation (8) in which subjects were required to breathe deeply a mixture of 50% oxygen and 50% nitrogen prior to cessation of breathing. Although breath-holding durations in that study (8) were observed to be longer in healthy control subjects than in both panic disorder and a mixed group of patients with other anxiety disorders, there were no differences observed between the two patient groups. We thought that our simple manipulation would mimic the sensation of impending suffocation to a degree, while allowing subjects the possibility of escape. We hypothesized that if a false suffocation alarm was active in panic disorder, then patients with panic disorder would attempt to escape sooner (i.e., have shorter breath-holding durations) than comparison groups of healthy subjects and patients with a different anxiety disorder (e.g., generalized social phobia).

METHOD

Patients with panic disorder (N=23; mean age=36.1 years, SD=8.5; 26% men [N=6]) and generalized social phobia (N=10; mean age=38.5 years, SD=9.7; 60% men [N=6]) were interviewed by using a modified version of the Structured Clinical Interview for DSM-III-R—Patient Version (SCID-P) (9) and diagnosed as meeting applicable DSM-III-R criteria. No patient met criteria for a current diagnosis of major depression or had a significant coexisting medical illness. Patients were instructed to remain medication-free prior to testing; however, we did not document compliance with this request by screening urine or plasma for benzodiazepines or antidepressants. Therefore, it is possible, according to patients' reports of prestudy medication consumption, that as many as four of the 33 patients disregarded our request and continued to take medication up to (but not including) the day of study. Healthy comparison subjects (N=26; mean age=37.0 years, SD=10.6; 35% men [N=9]) were screened by using a version of the SCID-P and were determined to have no lifetime axis I diagnoses, history of mental illness in first-degree relatives, or coexisting medical illness. All subjects completed a questionnaire assessing fear of anxiety symptoms (10) and provided informed consent prior to participating in the study.

Subjects reported to the laboratory at 9:00 a.m. Each subject was seated while an investigator (blind to diagnosis) applied ECG electrodes, rib cage and abdomen strain gauge belts for measurement of respiratory excursion, nasal cannula for capnographic sampling of

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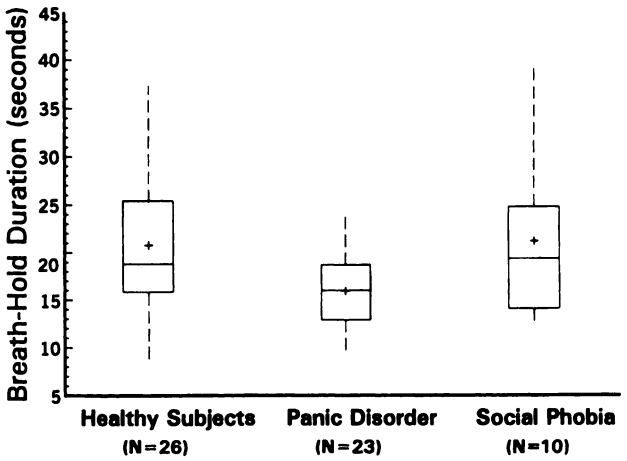
end-tidal CO_2, and an automated blood pressure cuff for monitoring blood pressure. Respiratory sinus arrhythmia—an index of cardiac vagal tone—was quantified by measuring the mean maximal heart period difference in successive breath-to-breath intervals between inspiratory and expiratory phases of the breathing cycle (11).

A 30-minute acclimatization period, with subjects recumbent, preceded the breath-holding test. The breath-holding test constituted three trials comprising a 1-minute anticipation period, cessation of breathing at functional residual capacity for maximum duration, and a 2-minute recovery period. Subjects were instructed to stop breathing following a normal (i.e., not forced) exhalation and to maintain the cessation for as long as possible. Compliance with the breath-holding instructions was monitored continuously through observation of recordings of end-tidal CO_2 and respiratory excursion. A 10-minute recovery period followed the breath-holding test. Subjects then underwent several other respiratory manipulations (e.g., Valsalva maneuver, paced respiration). The instructional set provided to the subjects did not suggest that the procedures were likely to be anxiogenic or panic-inducing.

FIGURE 1. Breath-Holding Durations of Healthy Subjects, Patients With Panic Disorder, and Patients With Social Phobia[a]



[a]+=mean, box=first to third quartile (i.e., interquartile range), horizontal line=median, dashed vertical lines=extension to last observed value within a distance of 1.5 times the interquartile range.

RESULTS

There were no between-group differences in levels of habitual aerobic exercise (12). We were, therefore, reasonably confident that any observed differences in breath-holding duration or cardiorespiratory reactivity would be due to factors associated with clinical status and not cardiovascular fitness.

Data presented represent mean values collapsed across trials and, for physiologic data, over specific time periods. A one-way analysis of variance (ANOVA) (two-tailed) of the breath-holding data revealed a significant main effect of diagnosis ($F=3.34$, $df=2, 58$, $p<0.03$). The means for this effect are presented in figure 1. Post hoc analyses were carried out by using Student-Newman-Keuls test (13). This analysis indicated that patients with panic disorder maintained breath-holding for significantly shorter durations (16.1 seconds, SD=3.7) than either healthy subjects (20.7 seconds, SD=7.2) ($df=56$, $p<0.05$) or patients with social phobia (20.8 seconds, SD=8.3) ($df=56$, $p<0.05$). Healthy subjects and patients with social phobia did not differ significantly in breath-holding duration.

Physiologic data (heart rate, vagal tone, respiratory frequency, and end-tidal CO_2) collected during the breath-holding procedure were analyzed in a 3×2 (Diagnosis by Time: pre- versus postbreath-holding) ANOVA with repeated measures on the last factor. There were no significant main effects of diagnosis (all F values <2) and no Diagnosis by Time interactions (all F values <1), indicating that patients and comparison subjects did not differ significantly in their patterns of cardiorespiratory responsivity to the task. An important finding was that mean end-tidal CO_2 levels before and immediately after breath-holding were similar in all three groups (before: panic disorder patients—33.5 mm Hg, SD=5.6; social phobia patients—37.3 mm Hg, SD=2.1; healthy subjects—35.1 mm Hg, SD=5.2; $F=2.0$, $df=2, 58$, n.s.; after: panic disorder patients—33.0 mm Hg, SD=5.6; social phobia patients—36.6 mm Hg, SD=2.2; healthy subjects—34.8 mm Hg, SD=4.6; $F=2.1$, $df=2, 58$, n.s.). These observations indicate that 1) patients with panic disorder were not hyperventilating prior to breath-holding, and 2) patients with panic disorder did not become more hypercapnic during breath-holding than either comparison group.

Correlations were calculated between breath-holding duration and self-rated fear of anxiety symptoms. The correlation between these variables was not significant ($r=-0.01$, $df=57$, $p=0.91$). No subject had a panic attack or spontaneously reported increased subjective anxiety as a result of the breath-holding procedure.

DISCUSSION

We found, as hypothesized, that patients with panic disorder held their breath for shorter durations than did either healthy subjects or patients with social phobia. On the other hand, physiologic responses to the breath-holding challenge did not differ among groups.

One interpretation of these data is that patients with panic disorder truncate breath-holdings prematurely in order to avoid activation of an evolved suffocation alarm (7). Indeed, the effects of prolonged cessation of breathing involve, among other things, several factors that have been linked to the occurrence of panic attacks—primarily hypercapnia (6) and air hunger (14). Since escape from voluntary breath-holding is readily available, breathing resumes prior to occurrence of these effects. Our finding that patients with panic disorder terminate breath-holding sooner than comparison subjects could, therefore, be considered evidence in favor of a pathologically lower activation threshold of the suffocation alarm in panic disorder (7).

Alternatively, we cannot discount that patients with panic disorder may terminate breath-holding sooner

not because of a pathological suffocation alarm, but simply in order to avoid unpleasant anxiety sensations that have been associated with the occurrence of panic attacks (15). However, we believe this scenario unlikely given the lack of relationship between breath-holding duration and fear of anxiety symptoms. If breath-holding was truncated in order to avoid unpleasant anxiety sensations, then we would expect a high correlation between these variables.

The current results, while preliminary, are intriguing. Further investigation of a false suffocation alarm in panic disorder may lead to a better understanding of the disorder and related treatment strategies.

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