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Symptom Specificity in Patients with Panic

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Thirteen patients with panic disorder with predominantly cardiorespiratory (CR) symptoms were compared with seven patients with predominantly gastrointestinal (GI) symptoms in an experimental procedure that involved exposure to phobia talk and voluntary hyperventilation (VHV). The CR patients had not only higher baseline anxiety, but also during phobia talk had a greater fall in pCO_2 and reported more respiratory symptoms than the GI patients. Moreover, the CR group found VHV more unpleasant and more like their panic attacks than the GI panickers, and reported more physical symptoms after it. These findings suggest that patients with PD are not only heterogeneous with respect to the system to which panic symptoms refer (CR or GI) but that provoking arousal in one system is more likely to produce distress if that system is the major focus of complaint. These findings, if replicated, would not support the suggestion that panic disorder is a uniform illness.

The symptoms of panic according to DSM–III–R (American Psychiatric Association, 1987) are referable to a number of body systems – respiratory, cardiovascular, neurological, and gastrointestinal. Associated with the panic symptoms are characteristic catastrophic cognitions. Hibbert (1984) claims that the connection between a patient's particular cluster of somatic symptoms and accompanying cognitions are "understandable"; for instance, those who experience palpitations, chest tightness and breathlessness interpret these symptoms as a heart attack. If such specificity exists it might explain the inability of any single challenge test (lactate infusion, yohimbine, caffeine, carbon-dioxide inhalation or hyperventilation) to induce panic in all patients with panic disorder (PD) (Clark & Hemsley, 1982); quite simply, the physiological changes produced might not mimic the somatic symptoms of a panic closely enough to provoke the catastrophic cognition.

It has been known for many years that: (a) individuals tend to respond to stress with their own 'specific' pattern of autonomic activation, arousal for an individual being maximal in the same physiological function whatever the stressor (Lacey *et al*, 1953); and (b) in patients with psychosomatic complaints "the particular physiological mechanism of that complaint is specifically susceptible to activation by stressful experience" (Malmo & Shagass, 1949).

Hyperventilation causes a characteristic array of physical symptoms (Bass *et al*, 1987) and produces a greater degree of distress in panic patients than in normal controls or patients with generalised anxiety (Rapee, 1986). Many PD patients have panic symptoms referable to the cardiovascular (Klerman, 1986) and respiratory (CR) systems. Lydiard *et al* (1986) drew attention to a subgroup of patients meeting criteria for PD whose principal somatic symptoms were gastrointestinal (GI) (abdominal pain, abdominal cramping, flatulence, urge to defaecate and diarrhoea) and whose reason for avoidance was fear of being faecally incontinent. These patients provide an intriguing opportunity to test a number of hypotheses.

This study compares the subjective and physiological responses of these two groups of panic patients (with predominantly CR and predominantly GI symptoms) to a psychological stressor and voluntary hyperventilation (VHV) and poses two questions.

(a) Will the two groups respond with equal distress to VHV, which produces sensations which are more referable to the CR than GI system?
(b) Will a psychological stressor produce reports of symptoms and physiological changes maximal in the system of principal complaint (i.e. either GI or CR) in the two groups of patients with PD?

Method

Patients were drawn from consecutive referrals to the authors' units. All met DSM–III–R criteria for PD with agoraphobic avoidance confirmed by interviews with psychiatrists trained in the use of the Upjohn version of the Structured Clinical Interview for DSM–III (SCID–UP; Spitzer & Williams, 1983).

Group I (CR) consisted of 13 patients whose panic symptoms were predominantly cardiovascular and respiratory, and whose fears during panic were of impending death, heart attack, or collapse. All 13 reported at least three of the following four symptoms (listed in DSM–III–R) during one of their panic attacks: shortness of breath (dyspnoea); choking or smothering sensations; palpitations or accelerated heart rate (tachycardia); chest pain and discomfort.

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Group II (GI) comprised seven patients whose panic symptoms were predominantly gastrointestinal. In addition to panic, all reported: abdominal discomfort; abdominal cramps; tenesmus; and diarrhoea, and fears of faecal incontinence during a panic attack.

The groups were of unequal size because of the small number of GI patients referred to the units. In a retrospective study (unpublished data), over ten years the GI patients comprised approximately 10% of agoraphobic referrals.

On the same day, before testing, the following ratings were made:

(a) the Fear Questionnaire (Marks & Matthews, 1979) – 15 self-rated items yielding three subscales (agoraphobia, blood-injury phobia, and social phobia), each with a range of 0–40 (higher scores denoting more anxiety and avoidance)
(b) the 90-item Symptom Checklist (SCL-90; Derogatis *et al*, 1973)
(c) a checklist of 37 self-rated symptoms clinically related to hyperventilation, for which subjects were asked if they had experienced any of them during the past week (Grossman & DeSwart, 1984).

During the experimental procedure a nasal catheter sampled end-tidal pCO_2 and measured respiratory rate; electrodes attached to ankles and wrists recorded heart rate. A box with nine buttons numbered 0 (complete calm) to 8 (panic) placed in front of the subjects allowed them to rate anxiety at a signal from the experimenter. Permanent tracings of pCO_2, respiratory rate, heart rate, and subjective anxiety were recorded on a polygraph.

Full details of the laboratory procedure are given in a separate report (Bass *et al*, 1989). Briefly, after clinical ratings subjects were taken into the laboratory, seated upright in a comfortable chair, had electrocardiograph electrodes and nasal catheter attached, and were shown how to rate subjective anxiety. Patients were acclimatised for five minutes and then told about the experiment:

> "This experiment studies how a certain bodily function behaves at rest and in response to certain tasks and instructions. I will be talking to you during the next 25 minutes and will ask you to do certain things. I want you to signify at specified times how anxious you feel by pressing a button in front of you. You will be debriefed at the end."

Details of the provocation test and the word 'panic' were omitted. The two stressors were phobia talk and VHV.

(a) *Phobia talk*. After five minutes' silence, patients were asked to imagine a phobic scene taken from the top of their hierarchy of feared situations (this scale had been determined at an earlier interview). For five minutes the experimenter described the fearful situation, emphasising stimulus propositions rather than response propositions (Lang, 1979). That is to say, images of a phobic scene such as a crowded supermarket, standing in a queue, etc., were described (stimulus content) as opposed to physical symptoms of anxiety such as trembling and incontinence (response content). This was done because emphasis on response propositions might spuriously provide evidence for specific physiological activation.
(b) *Voluntary hyperventilation (VHV)*. After a further five minutes of silence, subjects were asked to overbreathe at a rate of 30–40 breaths per minute for three minutes, after which they were requested to stop overbreathing.

The two provocation tests were presented in the same order for all subjects (phobia talk followed by VHV) as it was anticipated that hyperventilation may produce changes in respiratory variables that would be slow to return to baseline.

After each provocation test subjects were asked again to complete the 37-item check-list for any symptoms experienced during the test. For technical reasons this check-list was not completed by three patients from group I after phobia talk and one patient from group I after VHV. After the phobia talk, subjects were asked to rate their clarity of visual imagery (0 (none) to 8 (total)) and after VHV all subjects completed a hedonic visual-analogue scale ranging from 0 "the most pleasant feeling ever experienced" to 10 "the most unpleasant feeling ever experienced." After VHV, subjects were also asked to rate on two five-point scales: "How many of the complaints that brought you to the doctor were reproduced?", and "How similar were the symptoms produced during the overbreathing to those you experienced in the agoraphobic/panic situation?" Higher scores denote closer similarity. The procedure and timing of measures are outlined in Table I.

TABLE I

Ratings	*Sequence of procedures: min*											
	Baseline		*Phobia talk*			*Rest*		*VHV*[1]			*Recovery*	
	1	*4*	*6*	*8*	*10*	*11*	*14*	*16*	*17*	*18*	*19*	*23*
Subjective anxiety	X	X	X	X	X	X	X	X	X	X	X	X
End-tidal pCO_2	X	X	X	X	X	X	X	X	X	X	X	X
Respiratory rate	X	X	X	X	X	X	X	X	X	X	X	X
Heart rate	X	X	X	X	X	X	X	X	X	X	X	X
Hyperventilation checklist						X						X
Similarities questionnaire												X
Hedonic scale												X

1. Voluntary hyperventilation at 30 breaths/min.

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Baseline scores were obtained at four minutes (for phobia talk) and 14 minutes (for VHV), and changes from baseline of anxiety, pCO_2, respiratory rate and pulse rate were compared using two sample *t*-tests. Because of the heterogeneous variance between the two groups, the questionnaire scores and data from the hedonic scale and similarities scale were analysed using the non-parametric Mann–Whitney *U*-test. Comparison of checklist symptoms reported by the two groups was made using Fisher's exact probability test (two-tailed).

Results

The GI patients were younger than the CR patients and had shorter duration of symptoms (but closely similar ages of onset – approximately 25 years). They were also less severly ill, with lower scores on the social phobia and agoraphobia scales of the Fear Questionnaire and certain factors of the SCL-90 (Table II).

The CR patients were more anxious than the GI group throughout the experiment (Fig. 1), but increases in anxiety from baseline were not significantly different during phobia talk or VHV. CR patients had significantly lower pCO_2 levels at rest and their pCO_2 fell significantly more than that of the GI patients during and after phobia talk (at 8, 10 min and 11 min, $P<0.05$ for all; Fig. 1). During VHV both groups achieved a similar reduction in pCO_2: 15.5 mmHg for group I and 17.7 mmHg for group II. Respiratory rates were closely similar throughout the procedure, but heart-rate responses were markedly different during and after VHV. Surprisingly, the GI panickers showed significantly greater increase in heart rate at 18 minutes than the CR panickers ($P<0.01$).

Panic patients in the CR group reported five of the 37 symptoms from the 37-item check-list significantly more often than those in the GI group: unable to breathe deeply

TABLE II
Demographic and psychiatric data (medians and ranges) in the two groups of panic patients

	Group I Cardio-respiratory (n = 13)	*Group II Gastro-intestinal (n = 7)*
Age: years	40.0 (21–60)	29.0 (25–44)
Duration of symptoms: years	12.0 (2–41)*	6.0 (2–12)
SCL-90 scores		
Somatisation	17.5 (1–37)*	5.0 (3–18)
Obsessional–compulsive	11.0 (1–31)*	3.0 (1–13)
Interpersonal sensitivity	7.0 (0.28)*	1.0 (0–13)
Depression	17.0 (0–39)	8.0 (2–26)
Anxiety	22.0 (5–34)*	9.0 (3–16)
Anger–hostility	1.5 (0–11)	2.0 (0–6)
Phobic anxiety	17.0 (5–28)**	9.0 (3–16)
Paranoid ideation	1.5 (0–12)	0 (0–3)
Psychoticism	3.0 (1–18)	2.0 (1–9)
Fear questionnaire scores		
Agoraphobia	30.0 (12–34)**	16.0 (0–24)
Blood-injury phobia	16.0 (7–28)	8.0 (0–34)
Social phobia	14.0 (0–22)**	4.0 (2–12)

*$P<0.05$, **$P<0.01$ (Mann–Whitney *U*-test).

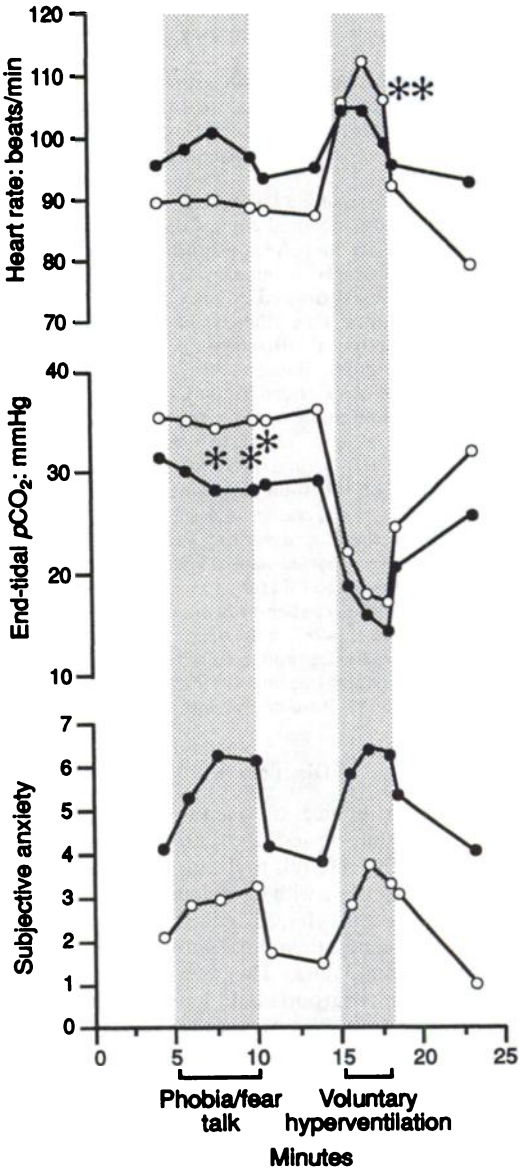


FIG. 1. Ratings of subjective anxiety, end-tidal pCO_2 and heart rate in 13 cardiorespiratory panickers (●—●) and 7 gastrointestinal panickers (○—○). Baseline scores are at 4 minutes for phobia talk and 14 minutes for VHV, and changes from baseline of anxiety, pCO_2 and heart rate were compared using two sample *t*-tests (*$P<0.05$, **$P<0.01$).

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enough; irregular heart beat; and tingling in fingers (all $P<0.05$); chest pains around heart region ($P<0.02$); and rapid heartbeat ($P<0.01$).

During phobia talk the following somatic symptoms on the symptom check-list were reported more often by the CR patients: unable to breathe deeply enough (7/10 v. 1/7; $P<0.05$); faster or deeper breathing than normal (8/10 v. 1/7; $P<0.02$).

Only one of the seven GI patients reported fear of incontinence and abdominal cramps during phobia talk. This patient was anxious before the experiment and elevated baseline arousal carried over into phobia talk. Subsequently, this patient became distracted by VHV, during which she became less anxious. One other GI patient said that she may have felt physical discomfort if phobia talk had continued beyond ten minutes.

After VHV there was a trend for the CR patients to report more symptoms referable to the respiratory system than those in the GI group, viz. unable to breathe deeply enough (5/12 v. 0/7; $P=0.1$), and need for air (4/12 v. 0/7; $P=0.2$). None of the four gastrointestinal complaints (abdominal discomfort, cramps, tenesmus, and diarrhoea) were reported by the GI group during VHV, but one patient from both groups reported nausea (NS).

CR patients tended to find the experience of VHV more unpleasant than the GI patients (median 96 (range 52–100) compared with 65 (18–98) on the hedonic scale; $P=0.09$), and found the experience produced sensations more similar to their normal panics (median 4.0 (range 2–5) compared with 3.0 (1–4) on the five-point similarities scale; $P<0.05$).

Discussion

The clinical differences between the two groups of patients were unexpected. Both groups were drawn from consecutive referrals to the same hospitals, and it is unclear why those with gastrointestinal complaints should have been referred a median of 11 years earlier in their illness than those with cardiovascular/respiratory complaints. The greater duration of illness in the latter group might have explained why their illnesses were so severe – as indicated by many factors of the SCL-90 and Fear Questionnaire.

The higher levels of subjective anxiety both at rest and during provocations probably reflect this greater level of morbidity in the CR group (though some of the physiological measures were similar at rest). Differences in tonic anxiety are an almost inevitable confound in panic-induction studies and make interpretation difficult (Margraf *et al*, 1986). With this in mind, the CR patients responded to phobic talk with a greater fall in pCO_2 and reported more respiratory symptoms than the GI group, and the specific symptoms reported more frequently were those directly referable to respiration.

Both groups overbreathed to a similar extent when instructed to hyperventilate (as judged by fall in pCO_2). The CR group clearly found the experience more unpleasant, reporting greater distress on the hedonic scale and reporting more physical symptoms. As during the phobia talk, the symptoms more commonly reported during VHV were those directly related to breathing. The CR group also found the sensations produced by VHV to be more like those experienced during a panic. These findings would lend some support to a suggestion that patients with PD are not only heterogeneous with respect to the system to which panic symptoms refer (cardiovascular/respiratory, gastrointestinal, or neurological) but that provoking arousal in a system is more likely to produce distress if that system is the major focus of complaint.

This hypothesis clearly needs further testing with larger numbers of patients controlled for duration and severity of illness. If these findings are replicated and, say, panic in patients with GI symptoms is provoked by colonic distension, in those with dizziness and light-headedness by hypotensive drugs, etc., it would clearly have implications for classification, treatment and theories of aetiology of PD. It would be difficult to support the suggestion that PD is a uniform illness (as indicated by DSM-III-R) caused by a metabolic disorder (Sheehan & Sheehan, 1983) if merely provoking the feared symptoms can precipitate panics.

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