Treadmill Exercise Test and Ambulatory Measures in Panic Attacks

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Treadmill exercise test performance and ambulatory heart rate and activity patterns of 40 patients with panic attacks were compared with 20 age-matched controls (control group 1) and 20 nonexercising controls (control group 2). All patients underwent a symptom-limited exercise stress test. Panic attack patients and control group 1 wore an ambulatory heart rate/activity monitor for up to 3 days. Panic patients had a significantly higher heart rate at 4 and 6 METS than either control group. The max METS were 11.2 ± 2.3, 13.5 ± 2.3 and 11.2 ± 1.8 for the panic attack patients and control groups 1 and 2, respectively. One panic patient had ischemia on the treadmill at 12 METS. Panic patients had a significantly higher standing heart rate than controls. Furthermore, 11 of 39 panic patients had tachycardia on standing compared with 3 of 40 controls. Panic attack patients had higher wake and sleep heart rates than control group 1, but the differences were not significant. These results are consistent with autonomic dysfunction in panic patients but may also be due to differences in physical conditioning. The treadmill can be useful for reassuring patients and for identifying the rare patient with ischemia on exercise.

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Panic attacks are intense periods of anxiety characterized by rapid and often spontaneous onset and multiple symptoms.[1] During panic attacks, patients often believe that they will lose control, die or go crazy. The relation of the panic attacks to cardiovascular physiology and pathology has attracted considerable interest for a number of reasons. Whereas panic attacks may be accompanied by any number of symptoms, the most common symptoms are cardiovascular. For example, 1 study found that 68% of 175 diary-recorded panic attacks were accompanied by palpitations or accelerated heart beat, 30% by shortness of breath and 25% by chest pain.[2]

Such symptoms have lead investigators to examine the cardiovascular physiology of panic patients. Lader and Mathews[3] observed heart rate increases from 40 to 50 beats/min during 3 panic attacks recorded in the laboratory. Cohen et al[4] reported 2 cases of relaxation-associated panic attacks observed in their laboratory in which heart rate increased by 50 beats/min.

Similar increases in heart rate have also been observed in feared situations. For instance, Roth et al[5] monitored the heart rates of agoraphobics with panic attacks and matched nonanxious controls before and during a standard test walk in a shopping mall. Although the mean maximal heart rate during the test walk was 113 beats/min for agoraphobics compared with 97 for the controls, the baseline heart rates were similarly elevated and the changes during the walk were not significantly different. In fact, the most consistent laboratory difference between panic patients and controls are higher baseline levels of heart rate.

Because of the laboratory evidence for panic attack-related heart rate changes, researchers have recently started to systematically monitor panic attacks in the patients' natural environment. Several studies have shown heart rate increases during panic attacks.[6,7] In 1 ambulatory study, the mean maximal heart rate during panic attacks was 117 beats/min.[6] These elevated heart rates appear to be sinus tachycardias.[6] Increases in blood pressure and respiratory rate have also been observed during ambulatory panic attacks.[8,9]

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Although panic attack patients have elevated levels of heart rate in anticipation of feared situations and occasional episodes of very high heart rates associated with panic attacks, it is not clear if these patients have continually high heart rates (e.g., tonically high heart rates) compared with control patients, and if so, if the higher heart rates represent more activity or poorer physical conditioning. The purpose of this study was to compare average daily and sleep heart rates in panic patients and nonanxious controls. A second purpose was to determine treadmill performance in patients with panic attacks compared with controls.

Methods

Forty females recruited to participate in a study comparing medication treatments for panic disorder and agoraphobia were selected. Subjects underwent a Structured Clinical Interview for Diagnosis, Upjohn Version (R.L. Spitzer and J.B. Williams, New York State Psychiatric Institute, 1983). Patients who met the criteria for uncomplicated panic disorder, panic disorder with limited phobic avoidance, or agoraphobia with panic attacks were eligible for the study. (These 3 disorders are differentiated by the extent of avoidance present. Patients with uncomplicated panic disorder have panic attacks but no avoidance; patients with panic disorder with limited phobic avoidance have panic attacks, avoid some situations and perform other tasks with extreme fear; and panic attack patients with agoraphobia actively avoid many situations.) Patients then underwent a history and physical examination. Complete blood count, electrolyte, blood urea nitrogen, creatinine, serum glutamic oxoloacetic transaminase, serum glutamic pyruvic transaminase and creatine phosphokinase levels were measured, and thyroid tests and urinanalysis were performed. Patients who were pregnant or lactating, had a history of seizures or head trauma with unconsciousness, a history of alcoholism or substance abuse or renal, hepatic, cardiac, pulmonary, endocrine or collagen disease were excluded. Patients with isolated nonejection clicks were excluded. All patients were asked to be drug free for at least 2 weeks before testing and a blood screen for benzodiazepines was obtained. Subjects then completed a variety of psychological tests, kept a panic and activity diary and then underwent a treadmill test and ambulatory monitoring as discussed.

Two sets of controls were obtained: Control group 1 was recruited by advertisements in the mass media. However, because our control group subjects are often unusually fit, a control group 2 was selected from a study determining the physiologic effects of self-monitored home-based moderate-intensity exercise training in men and women.[10] These subjects were employees of the Lockheed Missile and Space Corporation and were recruited by way of printed announcements in the company newspaper. Subjects who had been involved in regular, vigorous physical activity in the prior 6 months, i.e., walking or jogging 20 or more minutes continuously 3 or more times per week, or participated in an active sport more than once per week, or reported anxiety on a self-report inventory

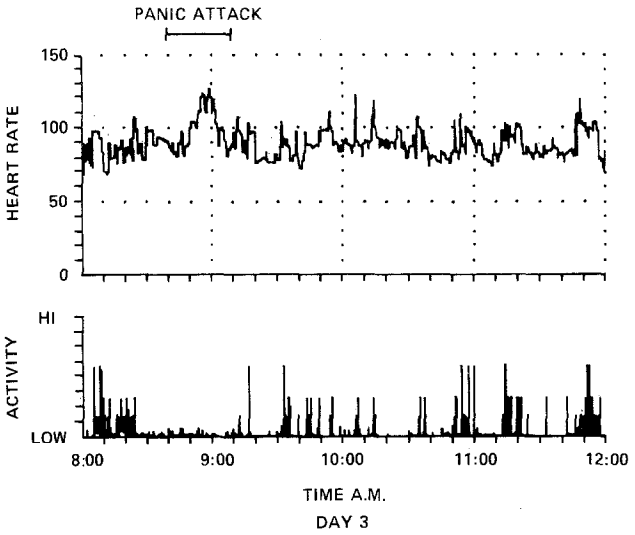

FIGURE 1. Period of increased heart rate not associated with increased activity. The patient reported a panic attack occurring between 8:40 and 9:10 A.M.

were excluded from the study. All subjects underwent a symptom-limited exercise test using a modified Balke protocol.[10,11] Panic attack patients and control group 1 subjects then wore a Vitalog MC-2 monitor for up to 3 days and nights (Vitalog Corporation). The MC-2 is a solid-state CMOS microcomputer that is interfaced to a read-only memory and a random access memory, a motion sensor, and an analog R-wave detector connected to the chest by electrocardiographic electrodes. The MC-2 measures 4 × 8 × 12 cm, weighs 0.5 kg, and is worn on a belt. The motion sensor, which is attached to the lateral thigh by an elastic band or tape, consists of 6 liquid mercury switches aligned on the faces of a cube. Figure 1 shows the heart rate/activity pattern recorded during a typical panic attack. Panic attack patients and controls also wore a Holter Monitor or Medicomp recorder for up to 24 hours. These data will be presented in a subsequent study.

The MC-2 microcomputer is programmed to store data on 8 levels of physical activity representing a total number of activations of the mercury switch over a predetermined period. One-minute samples of physical activity were used for this study. The total number of heart beats per minute during 1-minute periods was then stored in 1 of 64 bins, each representing about 2 beats/min over the range of 40 to 160 beats/min, with an additional bin for heart rates less than 40 beats/min and 1 for heart rates of 161 beats/min. At the end of data collection, the memory was loaded into a minicomputer for storage and analysis.

The average daily heart rate and activity were determined by averaging the minute by minute total heart rate and activity for waking hours after data were edited. Wake hours were determined by self-report from the diary matched with heart rate activity patterns suggesting ambulatory activities. Periods of no heart rate were edited out. Mean sleep heart rate was determined by averaging heart/activity patterns compatible with sleep and self-report.[12] Average daily

TABLE I Exercise Test Variables

	Panic Patients (40)	Control 1 (20)	Control 2 (20)
Rest HR	73 ± 11	70 ± 10	72 ± 12
4 MET HR	133 ± 20*	116 ± 20	123 ± 15
6 MET HR	149 ± 19	130 ± 20	138 ± 17
Max HR	175 ± 14	177 ± 17	177 ± 14
Max METs	11 ± 2	14 ± 2†	11 ± 2
Ischemia	1	0	0

Number of subjects are in parentheses. Values are mean ± standard deviation.

* $p < 0.01$ panic vs control groups 1 and 2 combined; † $p < 0.05$ control group 1 vs panic patients and control 2.

HR = Heart rate (beats/min); Max HR = heart rate at maximal workload on the exercise test; Max METS = maximal workload achieved.

TABLE II Heart Rate and Blood Pressures Changes on Standing

	Panic Patients (40)	Control 1 (20)	Control 2 (20)
Supine HR	73 ± 11	70 ± 10	72 ± 12
Standing HR	89 ± 15*	85 ± 14	80 ± 12
Supine SBP	113 ± 14	113 ± 13	110 ± 16
Standing SBP	117 ± 15	115 ± 14	110 ± 19
Supine DBP	71 ± 11	70 ± 8	70 ± 16
Standing DBP	77 ± 9	77 ± 9	73 ± 11

Number of subjects are in parentheses. Values are mean ± standard deviation.

* $p < 0.05$ panic compared with control group 1 and 2 combined.

HR = heart rate (beats/min); SBP = systolic blood pressure (mm Hg); DBP = diastolic blood pressure (mm Hg).

heart rate and sleep heart rate data were not evaluable in 3 patients.

The psychological tests included the Hamilton Anxiety,[13] Depression Inventory,[14] and the SCL-90.[15] The SCL-90 phobia scale, total number of panic symptoms from the SCID-UP and data from the panic attack diaries were used to characterize 3 critical features of the disorders: avoidance, number of somatic symptoms during panic attacks and number of panic attacks. A somatic symptom scale was constructed to measure cardiovascular awareness. Subjects reported how aware they were of cardiac symptoms on a Likert-type scale of 0 (not at all aware) to 7 (very aware).

The mean age of panic attack subjects was 36.7 ± 10. The mean age of subjects in control group 1 was 34 ± 9, and 43 ± 12 in control group 2.

Data Analysis

To adjust for conditioning effects, treadmill heart rates were analyzed by analysis of covariance with the max METS as a covariate and combining groups 1 and 2. Analysis of variance was used for other group comparisons.

Results

Treadmill data (Table I): Panic attack patients had significantly higher heart rates at submaximal effort, i.e., 4 and 6 METS than either control group. No differences in baseline or heart rate at peak workload were noted between groups. Patients and control group 2 subjects achieved significantly lower peak workload than subjects or control group 2. One panic patient reported a panic attack during the treadmill but continued to a high peak workload of 11 METS. Another subject had evidence of treadmill-induced ischemic ST-segment depression at 12 METS.

TABLE III Ambulatory Heart Rates

	Panic Patients (37)	Control 1 (19)
AVDHR	87 ± 8	85 ± 8
Sleep HR	67 ± 6	66 ± 10

The number of patients are in parentheses. Values are means ± standard deviation.

AVDHR = average daily heart rate (in beats/min) while awake; Sleep HR = average heart rate during sleep.

TABLE IV Ambulatory Heart Rates, Activity and Diagnosis

	No.	AVDHR	AVDACT
Uncomplicated panic disorder	10	85 ± 7	2.4 ± 1
Panic disorder with LPA	21	90 ± 8	2.3 ± 1
Agoraphobia with panic attacks	6	80 ± 7*	1.4 ± 1

Values are means ± standard deviation.

* $p < 0.01$, agoraphobia compared with other diagnoses.

AVDACT = average daily activity; AVDHR = average daily heart rate (beats/min); LPA = limited phobic avoidance.

Supine-standing heart rate and blood pressure (Table II): Heart rates on standing were significantly higher in panic patients than in control subjects. Furthermore, 28% (11 of 39) of the panic patients had tachycardia (>100 beats/min) on standing compared with 5% (1 of 20) in control group 1 and 10% (2 of 20) in control group 2 (chi-square <0.05 in patients compared with control groups.)

Ambulatory heart rates (Table III): A mean of 11.1 ± 2.7 and 11.3 ± 2.2 hours of average daily heart rate and activity were recorded for panic patients and control group 1 patients, respectively. A mean of 7.2 ± 1.8 and 7.6 ± 1.2 hours of sleep heart rate and activity were recorded for panic patients and controls, respectively. Panic patients were slightly less active during the day than controls (2.1 ± 0.8 vs 2.3 ± 0.5, mean activity levels for panic and control group 1 patients, respectively.) Panic patients had higher average daily heart rate and sleep heart rates compared with control group 1 and were less active, but the means were not significantly different. The average daily heart rate and sleep heart rates were compared in patients with tachycardia during standing to those with no tachycardia during standing. The mean average daily heart rate was significantly higher in patients with supine-standing tachycardia than patients without tachycardia during standing (94.0 ± 24 vs 84.8 ± 12, $F = 10.7$, $p = 0.003$), although there were no significant differences for sleep heart rates (69.0 ± 31 vs 66.3 ± 34).

Table IV shows that patients with agoraphobia have significantly lower heart rates than the other 2

diagnoses. Agoraphobics were also less active, the differences approaching significance (overall F = 3.04, p <0.06].

Symptoms (Table V): The total number of somatic symptoms during panic attacks, frequency of panic attacks and avoidance are critical features of panic disorder and agoraphobia. Pearson correlations were obtained between these measures and the physiologic data. Patients with more attacks had significantly lower peak treadmill workload and small changes in systolic blood pressure (but not heart rate) on arising. Phobic avoidance was inversely correlated with activity, as would be predicted; more phobic subjects are less active. Change in systolic blood pressure on standing was weakly correlated with total symptoms and avoidance, directly related to cardiovascular awareness and inversely related to the number of panic attacks.

TABLE V Correlations Between Self Report and Physiologic Variables

	SUPHR	DHR	DSBP	Max Mets	Wake HR	Wake Act
Total sym	0.19	−0.03	0.25	−0.01	0.15	0.12
Attack freq	−0.07	0.20	−0.50*	−0.31†	−0.14	−0.05
SCL phobia	0.25	−0.01	0.25	0.06	−0.19	−0.33†
CVA awa	−0.10	0.17	0.45*	0.19	−0.04	−0.09

* $p < 0.005$; † $p < 0.05$.

Attack freq = frequency of panic attacks from panic attack diary; CVA awa = cardiovascular symptom awareness; DHR = change in heart rate from supine to standing; DSBP = change in systolic blood pressure from supine to standing; Max METS = maximal workload on exercise testing in METS; SCL phobia = phobic avoidance from the SCL-90; SUPHR = supine heart rate (beats/min); Total sym = total symptoms reported for typical panic attack; Wake Act = average activity while awake; Wake HR = average heart rate (beats/min) while awake.

Discussion

An important finding of this study is that patients with panic attacks can undergo a symptom-limited exercise treadmill test to workloads comparable to non-fit controls. Studies have reported that anxious patients are "exercise intolerant," i.e., even mild exercise is accompanied by very high heart rates and unpleasant symptoms.[16-18] It has even been argued that treadmill performance is meaningless in the presence of anxiety and depression.[19] Although panic patients may have higher than normal heart rates at submaximal workloads, they do not exhibit exercise intolerance, and the treadmill exercise test can be effectively used to characterize patients' cardiovascular status. These results are consistent with Crowe et al,[20] who found that anxiety neurotics without mitral valve prolapse (MVP) had max VO_2 on an exerise treadmill comparable to controls.

Consistent with laboratory studies,[5] we found that panic patients have a higher average daily and sleep heart rate than control patients, but the differences were not significant and may reflect differences in fitness. However, the fact that panic patients had significantly higher heart rates at submaximal treadmill test levels even when the max METS was used as a covariate argues for heart rate increases independent of fitness.

Standing tachycardia was present in a significantly higher percentage of panic patients than controls. Although no single test of cardiovascular reactivity can be used to substantiate the presence of autonomic dysfunction,[21] supine-standing heart rates >100 beats/min are unusual in the normal population and may be indicative of autonomic dysfunction.

Autonomic dysfunction has been reported for patients with panic attacks,[22] for patients who present with symptoms common to panic attacks but not necessarily with panic attacks,[23,24] and for patients with physical problems, like MVP associated with panic attacks.[24,25]

The evidence linking autonomic dysfunction to at least 1 group of patients with MVP is particularly intriguing,[25] because MVP is more prevalent in patients with panic disorder.[26] This subgroup had decreased stroke volume, which is associated with increased heart rate and vasoconstriction.[25] Chronic vasoconstriction may result in decreased plasma volume and decreased ventricular volume that accentuate the tendency to a reduced stroke volume. This mechanism could lead to chronically elevated heart rates. Perhaps patients with MVP and panic share a common problem of autonomic dysfunction, which is manifested by both panic and MVP in some patients and either MVP or panic in others.

Several investigators have suggested a more precise characterization of this autonomic dysfunction. Gaffney et al[25] suggested that the problem, at least for MVP, lies in increased α-adrenergic activity. Charney and Heninger[22] argued that panic patients have abnormal regulation of noradrenergic function. They note that neuroanatomic and neurophysiologic evidence provides a basis for postulating a functional interaction between the activity of noradrenergic neurons in the spinal cord and medulla involved in cardiovascular regulation and forebrain neurons involved both in cardiovascular function and the behavioral expression of anxiety and fear.[27-30] The strong correlations observed between changes in systolic blood pressure on rising, cardiovascular awareness and panic attacks is consistent with this hypothesis. Studies now underway to examine long-term autonomic change in patients having significant symptomatic improvement will help clarify the importance of autonomic dysfunction in panic patients.

Conclusions

Panic patients have higher submaximal exercise treadmill heart rates but achieve the same peak treadmill performance as non-fit controls. Furthermore, panic patients have higher average daily heart and sleep heart rates than controls. Finally, a subgroup of panic patients had tachycardia during standing. Taken together, these findings are consistent with autonomic dysfunction in panic patients. The more precise nature of this autonomic dysfunction needs to be elucidated.

The exercise treadmill can be used to evaluate cardiovascular status of panic patients. Also, patients are very reassured when undertaking an exercise treadmill test to normal peak workloads.

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