Ambulatory Heart Rate Changes in Patients With Panic Attacks

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Of 33 "panic" attacks reported by patients wearing an ambulatory solid-state heart rate/activity monitor for 6 days, 19 (58%) occurred at heart rates disproportionate to activity levels and different enough from surrounding heart rates to indicate a distinct physiologic state. Intense panic attacks with three or more symptoms were the most readily identified. ECG monitoring found the elevated heart rates to be sinus tachycardias. Heart rate elevation did not occur during anticipatory anxiety episodes. Ambulatory heart rate recordings confirm the presence of major physiologic changes during self-reported panic attacks.

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A primary feature of panic disorder and agoraphobia is the occurrence of panic attacks. Changes in the frequency and intensity of such attacks are an important measure of the effectiveness of a treatment for these conditions. Unfortunately, measures of panic attacks in the natural environment have relied entirely on self-report; a more objective measure of panic attacks would obviously be desirable.

In theory, changes in heart rate could be an ideal measure of panic attacks, since cardiovascular symptoms, particularly symptoms suggesting acceleration in heart rate, are common during panic. Heart rate increases of 40–50 beats/minute have been reported in panic attacks observed during laboratory studies (1). Freedman et al. (2) found ECG heart rate increases of 16–38 beats/minute in seven of eight panic attacks during ambulatory monitoring; however, since activity was not measured simultaneously, it was not possible to determine if the heart rate increases were caused by increased workload on the heart. However, by combining an activity monitor with a heart rate monitor it is possible to differentiate periods of accelerated heart rate not due to physical activity from those due to other causes (3).

It is also of interest to determine if ambulatory heart rate patterns support the taxonomy of panic attacks proposed by Sheehan and Sheehan (4). They defined four categories of panic attacks or episodes: major spontaneous panic attacks of "devastating anxiety that come very suddenly" and are accompanied by three or more symptoms of panic, minor attacks accompanied by one or two symptoms, anticipatory anxiety episodes, and situational panic attacks, which are accompanied by three or more panic symptoms and follow an anticipatory anxiety episode. If there is an increase in heart rate during anticipatory anxiety, then situational panic attacks should be preceded by higher heart rates than are spontaneous panic attacks.

The major purpose of this study was to determine the correspondence between self-reported "panic" attacks and episodes of accelerated heart rate noted on the ambulatory heart rate/activity monitor. A related goal was to determine if these periods of elevated heart rate represent sinus tachycardia or other arrhythmias.

METHOD

Twelve female patients with self-reported panic attacks and 12 female control subjects without any history of panic attacks were recruited through mass media or referral from therapists to participate in the study. All subjects were screened by telephone for eligibility for the study. Panic attack subjects had to be age 18–60 years, not pregnant, willing to stop psychotropic medication, have had at least three typical panic attacks during a 3-week period, and have no active cardiovascular, renal, endocrine, or neurologic disease. Control subjects had to meet all of those criteria,

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except that they could have no panic attacks or any psychiatric disability. Informed consent was obtained from the subjects after the procedures had been fully explained.

The mean age of the patients was 39.8 years (compared to 35.5 years for the control subjects). Five patients and five control subjects were married; four patients and no control subjects were divorced.

Eligible patients underwent the Structured Clinical Interview for *DSM-III*-Upjohn Version (R.L. Spitzer, J.B. Williams, New York State Psychiatric Institute, 1983). Panic attack patients were required to meet *DSM-III* criteria for panic disorder or agoraphobia with panic attacks. A random 25% of the psychiatric interviews were videotaped for independent rating by two psychiatrists, who agreed on all diagnoses.

Following the psychiatric diagnostic interview, patients underwent a physical examination by a cardiologist, had an ECG, and underwent electrolyte, hematocrit, and BUN studies. Physicians also completed the 14-item Hamilton Anxiety Scale (5) and the 21-item Hamilton Depression Inventory (6).

Patients then wore a Vitalog MC-2 for 6 days. 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 ECG electrodes. (Information on the MC-2 can be obtained from the Vitalog Corp., 1058 California Ave., Palo Alto, CA 94306.) 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 six liquid mercury switches aligned on the faces of a cube.

The microcomputer is programmed to store data on eight 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 one of 64 bins, each representing about 2 beats/minute over the range of 40 to 160, with an additional bin for heart rates less than 40 and one for heart rates of 161 and above. At the end of data collection, the memory was loaded into a minicomputer for storage and analysis.

Patients were asked to record in a diary all attacks or anticipatory anxiety episodes occurring during the 6 days they were wearing the MC-2. Whenever they had an attack or episode they were asked when it began and ended, how intense it was (rated 0–10), what symptoms accompanied it, how long it lasted, and what they were doing during it. They were also asked to classify it as a major spontaneous attack (type 1), a minor attack (type 2), an anticipatory anxiety episode (type 3), or a situational panic attack (type 4). The diaries were reviewed every 3 days. In this paper "panic attack" will refer to types 1, 2, and 4 combined unless otherwise noted. "Episodes" will refer to anticipatory anxiety episodes (type 3).

On at least one day of Vitalog MC-2 recording, a Medicomp solid-state ECG monitor was simultaneously used both to validate the MC-2 heart rate recording and determine if the patient was having any arrhythmias. When possible, self-reported panic attacks or episodes were matched with MC-2 heart rates and Medicomp recordings.

With the Vitalog attached, patients underwent a treadmill test at four metabolic equivalents (METs), according to a Bruce protocol (7).

Agreement between Vitalog records and self-reports of panic attacks or episodes was analyzed using two sets of criteria: one for a definite MC-2 panic attack and the other for a probable MC-2 panic attack.

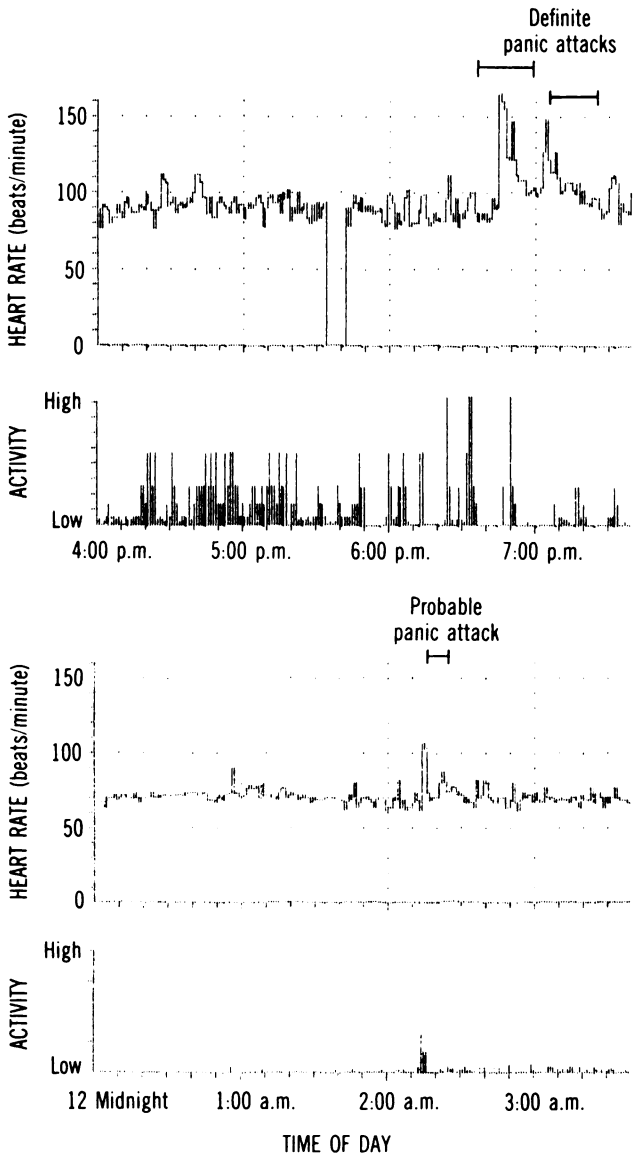
To determine a definite MC-2 panic attack, three observers blind to patients' status and diaries reviewed heart rate activity levels, looking for heart rate increases 1) of at least 30 beats/minute from surrounding 15-minute periods, 2) lasting at least 3 minutes, and 3) with little or no physical activity. These criteria were based on an earlier study (3). Only if all three observers agreed and if the event occurred within the exact time that subjects had reported in their diary was it scored as an agreement. Two self-reported panic attacks meeting the criteria for a definite MC-2 panic attack can be seen in figure 1.

Since many panic attacks and anticipatory anxiety episodes occur during periods of some activity, a second approach was developed to determine if heart rate/activity patterns during self-reported attacks or episodes were different from those during surrounding periods. Two observers assessed the heart rate/activity rate during a self-reported panic attack as meeting the probable criteria if 1) there was an increase in heart rate greater than 20 beats/minute above the surrounding 30-minute average, 2) the heart rate increase lasted at least 3 minutes, and 3) it was greater than expected from a response to comparable levels of activity. The two observers agreed in 85% of all cases; the remaining disagreements were resolved by a third observer. An example of heart rate/activity patterns fulfilling the criteria for a probable MC-2 panic attack is given in figure 1.

Panic attacks meeting the criteria for a definite or probable MC-2 panic attack were analyzed in terms of their duration (the time between the first rise of 10 beats/minute above baseline, i.e., mean heart rate 30 minutes before and after reported time of attack and the return to baseline levels), time of onset (the time between the first rise of 10 beats/minute and the time at which the maximum heart rate occurred), and time of offset (the time from the end of maximum heart rate to return to baseline).

Heart rate/activity patterns during self-reported panic attacks or episodes were compared to those during periods lasting the same intervals as the panic attacks or episodes but exactly 24 hours later (or before if the attack occurred on the last day) to determine specificity of patterns during self-reported panic attacks or episodes.

FIGURE 1. Heart Rate and Activity Level During Two Definite and One Probable Panic Attacks



RESULTS

The mean±SD Hamilton anxiety score for patients was 28.1±9.2; the mean Hamilton depression score was 15.8±10. The mean Hamilton anxiety score for control subjects was 1.0; the Hamilton depression score was less than 1.

Thirty-three panic attacks and eight anticipatory anxiety episodes were reported in the patients' diaries during MC-2 monitoring. Data on at least 5 days of 24-hour monitoring were available for all subjects. The control subjects reported no panic attacks and only four anxiety episodes, none of which was accompanied by more than one symptom. The characteristics of the 41 self-reported panic attacks and anticipatory episodes are given in table 1.

By self-report, situational panic attacks (type 4) were significantly more intense than other types of panic attacks (types 1 and 2) or anxiety episodes (see table 1). Anxiety episodes (type 3) occurred at significantly lower heart rates than did spontaneous (type 1) or situational (type 4) attacks. The intensity of panic attacks and anxiety episodes combined was significantly correlated with the duration (R=.31, p=.02) and maximum heart rate (R=.45, p=.003) during the recorded period. Duration and maximum heart rate were not significantly correlated. Intensity was not significantly correlated with the number of symptoms for the 33 panic attacks but was correlated when anxiety episodes were included.

The four categories of panic attacks and anxiety episodes occurred with apparent random distribution during the day, with the exception of spontaneous panic attacks (type 1), which had a relatively high frequency from 1:30 to 3:30 a.m., waking subjects from sleep (figure 2).

Across all panic attacks and episodes, the most commonly reported concurrent event was driving (N=10), followed by sleeping (N=6) and watching television (N=4).

Four of the 33 self-reported panic attacks in the diaries met the definite MC-2 criteria; two of them had been classified by subjects as major spontaneous attacks (type 1) and two as situational (type 4). An additional 15 self-reported panic attacks occurred with heart rate/activity patterns meeting the probable MC-2 criteria (table 1). Sixteen of these definite and probable attacks were classified by subjects as spontaneous (type 1) or situational (type 4) panic attacks; the remaining three were classified as minor spontaneous attacks (type 2). The 19 definite and probable panic attacks occurred at a significantly higher mean±SD heart rate (116.8±24.6) than the matched heart rates of 97.4±21.8 (t=2.6, p=.01) that occurred 24 hours before or after. For these 19 panic attacks, the mean±SD change in heart rate from the start of self-reported panic to peak heart rate on the MC-2 was 38.6±4.2 beats/minute. The time from the start of panic to peak heart rate was 4±2.7 minutes, and these heart rate changes lasted 20.2±1.3 minutes.

On the basis of the diaries, the 19 panic attacks that met the MC-2 criteria for definite or probable attacks were significantly more intense (mean±SD=4.7±4.45) than the 14 that could not be matched (mean±SD=3.3±4.1; t=2.2, p=.04), but they were not of significantly longer duration (mean=29.3±20 versus 22.7±32.5). There were no significant differences in heart rate symptom patterns between these two groups: cardiovascular symptoms were reported in 37% of the probable and definite panic attacks, compared to 29% of the panic attacks not associated with heart rate changes.

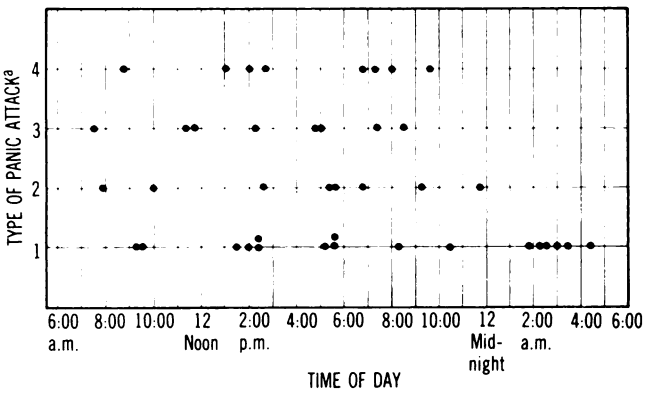
The percentage of each type of panic attack or episode that met the MC-2 criteria for a definite or probable panic attack was as follows: type 1, 65%; type 2, 38%; type 3, 0%; and type 4, 63% (see table 1).

TABLE 1. Characteristics of 41 Panic Attacks and Episodes Reported by 33 Patients

Type of Attack	Number	Intensity[a] Mean	Intensity[a] SD	Length (minutes) Mean	Length (minutes) SD	Heart Rate (beats/minute) Maximum Mean	Heart Rate (beats/minute) Maximum SD	Heart Rate (beats/minute) 10 Minutes Before Attack Mean	Heart Rate (beats/minute) 10 Minutes Before Attack SD	Number of Definite and Probable Attacks According to Ambulatory Monitor
Major spontaneous panic attack	17	3.9[b]	1.7	49.2	51.0	108.2	17.6	77.4	13.0	11
Minor spontaneous panic attack	8	2.5[c]	1.9	17.3	18.0	99.6	11.2	79.6	15.4	3
Anticipatory anxiety episode	8	3.3[d]	1.8	15.9	7.4	89.2[e]	8.9	74.1	20.0	0
Situational panic attack	8	6.3	2.5	30.4	38.9	117.4	30.0	88.4	10.0	5

[a]Rated on an 11-point scale; 0=none, 10=extreme.
[b]Significantly different from situational panic attacks ($t=3.0$, $df=24$, $p<.005$).
[c]Significantly different from situational panic attacks ($t=4.0$, $df=15$, $p<.005$).
[d]Significantly different from situational panic attacks ($t=3.4$, $df=15$, $p<.005$).
[e]Significantly different from spontaneous ($t=2.3$, $df=24$, $p<.05$) and situational ($t=2.1$, $df=15$, $p<.05$) panic attacks.

FIGURE 2. Time of Each of 41 Patient-Reported Panic Attacks and Episodes



[a]1=Major spontaneous panic attack, 2=minor spontaneous attack, 3=anticipatory anxiety episode, 4=situational panic attack.

In reviewing all of the MC-2 data, the raters identified 14 heart rate/activity periods that met the criteria for a definite panic attack. As previously mentioned, four of these occurred during self-reported panic attacks, leaving 10 false-positives. Seven false-positive probable or definite periods were identified on the normal subjects' MC-2 records.

The mean±SD heart rates for the 10 minutes preceding the panic attacks or episodes were 77.4±13, 79.6±15.4, 74.1±20, and 88.4±10 beats/minute for major spontaneous attacks, minor spontaneous attacks, anxiety episodes, and situational attacks, respectively. These were not significantly different.

Six panic attacks occurred during simultaneous monitoring of ECGs with the Medicomp. When elevated, the heart rate rhythm represented a sinus tachycardia; there were no apparent episodes of ST-T segment depression or arrhythmias other than sinus tachycardia.

The baseline and maximum heart rates during the treadmill test were not significantly different for patients and control subjects (72.1 and 121.3 beats/minute compared to 68.9 and 120.1 beats/minute, respectively). There were no arrhythmias or ischemic episodes during the treadmill test.

DISCUSSION

This study demonstrated that many self-reported panic attacks occur at heart rates disproportionate to activity levels and different enough from surrounding heart rates to indicate a distinct physiologic state. Panic attacks occurring with three or more symptoms, the so-called major spontaneous and situational types, met the MC-2 criteria for a definite or probable attack in 64% of the incidents. The elevated heart rates appear to represent a sinus tachycardia and not some other kind of arrhythmia.

The high level of agreement between the criteria for a definite or probable panic attack and the self-reported panic attacks suggests that ambulatory measures could be used to assess changes in the frequency of panic attacks. Nevertheless, problems exist with the current criteria. Ideally, all panic attacks would be identified by the definite criteria, but these criteria require little or no physical activity. Most panic attacks are accompanied by enough physical activity to produce some heart rate increase, and this increase must be adjusted to determine whether a heart rate episode is greater than would be expected for that level of activity and whether the heart rate pattern was different in other ways from surrounding episodes. That independent observers agreed in their ratings is evidence of the reliability of the criteria. The fact that matched heart rates occurring 24 hours before or after the definite or probable MC-2 panic attacks were significantly lower is further evidence that the criteria—and attacks—were unique physiologic events. Nevertheless, except for the definite episodes, we did not determine how many false-positives would be generated by these criteria—that is, how many probable episodes occurred that were not associated with self-report. This difficult task might be accomplished

by time series analysis of heart rate records or some other statistical procedure. An alternative method for future studies employing heart rate recordings would be to have subjects either rest or assume a very low activity level during panic attacks.

Are "panic" attacks (types 1, 2, and 4) different from anticipatory anxiety (type 3)? Our data suggest that subjects accurately differentiate between anticipatory anxiety and the other three kinds of attacks, since no anticipatory episode was associated with definite or probable MC-2 criteria. Of course, if anticipatory anxiety episodes are accompanied by small heart rate changes (e.g., less than 10 beats/minute), our methods would not be sensitive enough to detect them.

Are panic attacks distinguished best by the number of symptoms or intensity? Since intensity of panic attack is significantly correlated with number of symptoms and heart rate, it is not surprising that panic attacks with three or more symptoms—the so-called major and situational types—showed the greatest agreement with the definite or probable criteria. And yet 38% of the minor spontaneous attacks also agreed with the definite or probable criteria. The fact that normal subjects report one or two symptoms during frightening episodes suggests that it might be useful to employ three or more symptoms to differentiate panic attacks in patients from those in normal subjects. In favor of using the number of symptoms, rather than their intensity, to distinguish panic attacks is the observation that panic attacks meeting the definite or probable MC-2 criteria occur at very low levels of intensity. In favor of using intensity is the observation that some minor spontaneous attacks met the probable or definite criteria.

Do major spontaneous and situational panic attacks differ? There are no heart rate patterns distinguishing these two types of panic attacks. Situational attacks were more intense than major spontaneous attacks and occurred at higher heart rates. Heart rates before the spontaneous and situational panic attacks were similar, suggesting that buildup of heart rate is not a distinguishing feature of situational panic attacks.

Do normal subjects have panic attacks? One normal subject reported a fearful event that was accompanied by a heart rate/activity pattern which met the definite MC-2 criteria, but it was accompanied by only one symptom. No normal subjects reported more than two symptoms during fearful events. While this is consistent with some abnormality in panic patients not seen in normal subjects, it may also be that panic patients experience or report more symptoms in response to the same physiological or environmental stimulus. It is also puzzling that the same patient will have the different symptoms at different times and that types of symptoms are independent of the type of panic attack.

Finally, it is curious that many panic attacks are not accompanied by unique heart rate/activity patterns. This may be due to a number of reasons. First, the exact match criteria we used, in which the MC-2 heart rate changes had to occur within the self-report time period, were very strict. Since many subjects reported panic attacks beginning on the half hour, it is apparent that there is some inaccuracy of self-report. However, if we broaden the criteria to include heart rate/activity patterns within 1 hour of the panic attack, only six of the 22 self-reported panic or anxiety attacks that did not meet earlier definite or probable criteria would then meet these criteria, leaving 16 panic or anxiety attacks in which heart rate changes were simply not associated with MC-2 evidence of increased heart rate. Second, subjects might be experiencing premature ventricular contractions (PVCs) or other changes in cardiovascular function (e.g., cardiac output) rather than, or in addition to, heart rate changes. PVCs and active nonsinus arrhythmia were not associated with panic or anxiety attacks on the ECG ambulatory records, but other changes in cardiovascular function cannot be ruled out. Third, it is possible that at different times panic attacks occur with different physiologic changes, even within the same subject. Individual response specificity is well known, but changes in response pattern to the same stimulus over a relatively short time would be very unusual. Fourth, heart rate changes may represent a response to a panic attack rather than being the panic attack, so that the heart rate response occurs only with appropriate mediating events such as the patient's perception of the attack. Finally, such events might simply represent an error in reporting. If so, at least for spontaneous and situational attacks, this would represent an error rate of 35%–40%.

The occurrence of nighttime panic attacks may be one of the more important findings of this study. The most common time of the attack, from 1:30 a.m. to 3:30 a.m., represents the apex in many circadian hormone cycles. Is some aspect of the sleep cycle or the circadian rhythm associated with panic attacks—an effect that becomes more apparent at night?

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