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Motor Activity and Tonic Heart Rate in Panic Disorder

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Abstract. Motor activity and tonic heart rate were monitored in 62 drug-free panic disorder patients and 40 normal control subjects. Mean daily activity, mean waking heart rate controlled for activity, and mean sleeping heart rate were determined. Panic disorder patients without phobic avoidance showed higher activity than control subjects or patients with limited or extensive avoidance. Similarly, an "inverted U" relationship between trait anxiety and activity was observed. On the other hand, neither mean waking nor sleeping heart rate showed significant differences between patients and controls, suggesting that the differences previously reported in laboratory studies result from anticipatory anxiety.

Key Words. Panic disorder, trait anxiety, motor activity, heart rate.

Motor activity has been shown to have interesting relationships with abnormal behavior in a variety of psychiatric disorders, including depression (Kupfer et al., 1974; Wolf et al., 1985), mania (Weiss et al., 1974), anorexia nervosa (Falk et al., 1985), obesity (Chirico and Stunkard, 1960), and hyperactivity (Porrino et al., 1983), as well as correlations with personality characteristics (King et al., 1988). While motor activity has not been previously studied in anxiety disorder patients, an association between activity and anxiety has been reported in children, with lower activity being associated with interpersonal inhibition (Buss et al., 1980; Korner et al., 1985). Korner et al. (1985) also found that activity level was a relatively stable characteristic of individuals from 3 days of age to early childhood. Similar relationships have been observed in animals (Echandia et al., 1985; Newton et al., 1988). Activity may also be important to take into consideration in the study of heart rate (HR).

Studies of the autonomic changes occurring during panic attacks have confirmed that panic patients often show physiological changes consistent with their subjective somatic complaints (see Clark et al., in press, for review). Interest has subsequently

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focused on the possibility that tonic physiological variables reflecting arousal, such as tonic HR, may show differences between panic patients and controls. For example, Roth et al. (1986) compared 37 panic disorder patients with agoraphobia and 19 controls, who were similar to the patients in age, sex and race, and found that the patients had higher average baseline HR in the laboratory by approximately 12 beats per minute (bpm). These authors noted that this difference may have reflected a reaction to phobic elements of the laboratory situation such as an unfamiliar environment, restraint of movement, and relative isolation during HR measurement. In addition, the results were contaminated by the fact that 9 of the 37 patients admitted taking antianxiety drugs ($n = 6$) or alcohol ($n = 3$) within 12 hours of testing.

In an attempt to eliminate the confounding characteristics of the laboratory, Freedman et al. (1985) measured HR outside the laboratory using an ambulatory monitoring device. When HR was measured in this way over two 12-hour waking periods, differences in tonic HR between panic patients (HR = 78.3 ± SD 11.9 bpm, $n = 12$) and controls (HR = 78.4 ± SD 8.4 bpm, $n = 11$) were not observed. This difference between ambulatory and laboratory findings may be important. The study of Freedman et al. (1985) cannot be seen as definitive, however, due to the relatively small number of subjects and the lack of activity measurement. Furthermore, Freedman et al. (1985) did not consider the possibility that mean HR may be more closely correlated with stable individual differences in anxiety level, i.e., trait anxiety (Spielberger, 1983), than with whether an individual is diagnosed as having panic disorder. Differences between control subjects as well as between panic disorder patients on trait anxiety may be of interest in relationship to both mean activity and HR.

The purposes of this study were as follows: (1) to determine whether there were differences between control subjects and panic disorder patients, differentiated by degree of phobic avoidance, on motor activity and tonic HR, and (2) to examine the relationships of trait anxiety with motor activity and tonic HR. The study sought to minimize confounding factors by using only drug-free patients and control subjects, by using ambulatory monitoring to measure HR and activity outside the laboratory, and by controlling for activity in the analysis of HR. The possible influences of sex and body weight were also determined.

Methods

Subjects. Seventy-nine panic disorder patients and 42 control subjects were recruited from the mass media. The control group was selected to be similar in age and sex to panic disorder patients and was without significant psychiatric or medical disorders.

Control subjects and patients underwent a Structured Clinical Interview for *DSM-III* (Spitzer and Williams, 1983). Control subjects were eligible if they had no history of psychiatric disorders and were taking no psychoactive medications. Patients were eligible for the study if they had at least some spontaneous panic attacks, had panic attacks with four symptoms occurring during an attack, and had at least one panic attack each week for the past 3 weeks.

Patients were excluded for a primary diagnosis of major depression; for diagnoses of mania, cyclothymia, psychosis, obsessive-compulsive disorder, and alcohol or drug abuse; and if they were acutely suicidal. Patients meeting the screening criteria underwent a medical history,

physical examination, and routine laboratory tests. Patients with significant medical illnesses were excluded.

Measures of Phobic Avoidance, Trait Anxiety, and Depression. Experienced clinical interviewers classified patients as having panic disorder without avoidance if they exhibited no significant avoidance; panic disorder with limited phobic avoidance if they had significant avoidance of some phobic situations or endured phobic situations with dread; or panic disorder with extensive phobic avoidance if they had generalized travel restrictions, the need for a companion away from home, or a markedly altered lifestyle.

To determine the validity of the above categorization, patients were given subjective measures of phobic avoidance, phobic anxiety, and depression. A measure of phobic avoidance was derived from questions from the Marks-Matthews Fear Inventory (Marks and Matthews, 1979) pertaining to agoraphobic avoidance with two additional items—feeling trapped or caught in closed places and being left alone. Phobic anxiety was measured by the Symptom Checklist-90 (SCL-90; Derogatis, 1977) phobic anxiety subscale. The mean number of panic episodes per week was determined from patient diaries, and included anticipatory panic attacks, situational panic attacks, spontaneous panic attacks, and limited-symptom panic attacks (Taylor et al., 1986). Physicians reviewed diaries with subjects for completeness and face validity. The Beck Depression Inventory (BDI; Beck et al., 1961) was used as a measure of depression.

Both panic disorder patients and controls completed the trait scale of the State-Trait Anxiety Inventory (STAI; Spielberger, 1983). As the STAI was added after the study was begun, some subjects did not complete this measure.

Activity and Tonic Ambulatory HR Monitoring. Panic disorder patients and control subjects wore a Vitalog MC-2 activity and HR monitor for up to 3 days and nights. The Vitalog MC-2 (Vitalog Corporation, Mountain View, CA) is a solid state microcomputer with a motion sensor consisting of six liquid mercury switches aligned on the faces of a cube attached to the lateral thigh and an analog R-wave detector connected to the chest by electrocardiographic electrodes. Physical activity is categorized to eight levels representing logarithmic transformation of the number of activations of the mercury switch over each 1-min sample. Activity level and the number of heartbeats during each 1-min period are simultaneously stored. When data collection is completed, the memory is transferred to floppy disk for later analysis. Output may be viewed over specific time periods, with a concomitant display of physical activity and HR. The development of this device and further technical details have been described elsewhere (Taylor et al., 1982).

Data Analysis. Waking and sleeping periods were identified using activity level by a method similar to one previously described (Burnett et al., 1985), and the validity of the method was checked by patient diaries. Time periods with missing data or obvious artifacts (e.g., HR = 0) were excluded from the analysis. Where possible, the analysis began with the first sleep period, with the following waking period being used in most cases so that, for a given subject, the data came from the same 24-hour period. Activity and HR analyses were based on one waking and one sleeping period for each subject with an average of 11.5 (SD 2.8) hours for waking and 7.1 (SD 1.7) hours for sleeping for patients as compared to 11.7 (SD 2.3) hours for waking and 7.2 (SD 1.3) hours for sleep for controls.

In all analyses comparing patient groups and controls, patients were divided by degree of phobic avoidance, and all groups were compared by analysis of variance (ANOVA). Only when the ANOVA was statistically significant were multiple comparisons carried out by Scheffé's procedure (Scheffé, 1953). All minimum probabilities for significance tests were $p < 0.05$, with two-tailed tests used.

The possible effect of activity on sleeping HR was controlled by eliminating all time periods during sleep in which significant activity occurred. For waking HR, in addition to comparing

groups with a one-way ANOVA uncorrected for activity, an analysis of covariance (ANCOVA) was performed, with activity as a covariate. For correlations between waking HR and clinical measures, partial correlations controlling for activity were used. To test for possible confounding effects of body weight, mean body mass index (BMI: weight in kg divided by height in m^2) was calculated for each subject and statistical relationships with the primary variables determined. The possible effects of sex were also analyzed.

Correlations were calculated between trait anxiety and activity using control subjects and panic patients both separately and combined. To determine fit with a nonlinear model, a quadratic equation was developed by computer program (Statistical Package for the Social Sciences, PC version). The resulting equation was then compared to the data collected by regression analysis to determine the percentage of variance accounted for by the model.

Excluded Subjects and Missing Data. All patients were asked to discontinue any psychoactive medications for at least 2 weeks before testing. Blood samples were obtained from patients and controls. The serum analysis included diazepam, desmethyldiazepam, alprazolam, imipramine, and desmethylimipramine. Seventeen patients and two control subjects were found by serum analysis to be taking prohibited benzodiazepines or tricyclic antidepressants, and they were excluded from all analyses. The maximum number of subjects available for analysis was 40 controls, 17 panic disorder patients without avoidance, 35 panic disorder patients with limited avoidance, and 10 panic disorder patients with extensive avoidance.

For variables collected in both control subjects and patients, data were missing for activity (controls, $n = 1$; patients, $n = 3$), waking HR (controls, $n = 1$; patients, $n = 2$), sleeping HR (controls, $n = 7$; patients, $n = 4$), and STAI (controls, $n = 13$; patients, $n = 16$). For variables collected only in patients, data were missing for phobic avoidance ($n = 5$) and phobic anxiety ($n = 2$).

Results

Table 1 shows the age, sex ratio, BMI, and trait anxiety variables for control subjects and the three patients groups. These groups did not differ significantly in age or BMI, but there was a significant difference in sex ratio, with panic disorder patients without phobic avoidance having a somewhat higher proportion of males than the other groups. Trait anxiety was lower in control subjects than in all patient groups, and patient groups were not significantly different from each other.

Table 1. Age, sex, body mass index, and trait anxiety in controls and panic disorder (PD) patients categorized by degree of phobic avoidance (mean ± SD)

	Age	Sex ratio	Body mass index	Trait anxiety
1. Controls	35.9 ± 10.6	13% M 87% F	22.9 ± 4.7	32.4 ± 7.9
2. PD without avoidance	35.8 ± 10.2	47% M 53% F	24.2 ± 3.6	43.6 ± 9.8
3. PD limited avoidance	35.2 ± 8.4	26% M 74% F	23.5 ± 3.4	49.8 ± 11.8
4. PD extensive avoidance	30.1 ± 8.2	20% M 80% F	23.6 ± 1.7	53.7 ± 14.4
Test statistic; *df*, probability	$F = 1.0$; $df = 3, 97$; NS	$\chi^2 = 8.1$, $df = 3$, $p < 0.05$	$F = 0.4$; $df = 3, 91$; NS	$F = 15.3$; $df = 3, 69$; $p < 0.0001$
Significant comparisons (by Scheffé *F* test)	—	—	—	1 < 2, 3, 4

Table 2 shows the relationships between the categorization of panic disorder patients by degree of phobic avoidance and subjective measures of phobic avoidance, phobic anxiety, panic attacks, and depression. Panic patients without avoidance, with limited avoidance, and with extensive avoidance showed statistically significant differences by one-way ANOVA on phobic avoidance, phobic anxiety, and the BDI, but not on the frequency of panic attacks.

Table 2. Clinical measures in panic disorder (PD) patients categorized by degree of phobic avoidance (mean ± SD)

	Phobic avoidance	Phobic anxiety	Panic attacks	Beck Depression Inventory
1. PD without avoidance	3.7 ± 4.6	1.1 ± 1.9	4.6 ± 3.8	4.2 ± 3.3
2. PD limited avoidance	8.7 ± 5.1	7.9 ± 4.9	8.1 ± 6.2	7.4 ± 4.9
3. PD extensive avoidance	15.6 ± 3.1	10.8 ± 4.3	9.3 ± 7.3	8.2 ± 6.5
F ($df = 2, 54$), probability	17.5 < 0.0001	19.9 < 0.0001	2.7 NS	3.2 < 0.05
Significant comparisons (by Scheffé F test)	1 < 2 < 3	1 < 2; 1 < 3	—	None

Table 3 shows that panic disorder patients without avoidance had higher activity than control subjects (Scheffé $F = 5.3$, $p < 0.05$), patients with limited phobic avoidance (Scheffé $F = 3.5$, $p < 0.05$), and patients with extensive avoidance (Scheffé $F = 3.5$, $p < 0.05$). Other pairwise comparisons were not statistically significant. There were no significant differences between groups on sleeping HR, waking HR, or waking HR controlled for activity.

There were no significant differences between males and females on activity ($t = 0.83$, $df = 96$, $p =$ NS) or waking HR ($t = 0.21$, $df = 97$, $p =$ NS). There was a significant difference for sleeping HR (males: 62.2, females: 66.5, $t = 2.00$, $df = 89$, $p < 0.05$). Separate HR analyses for males and females, however, also failed to

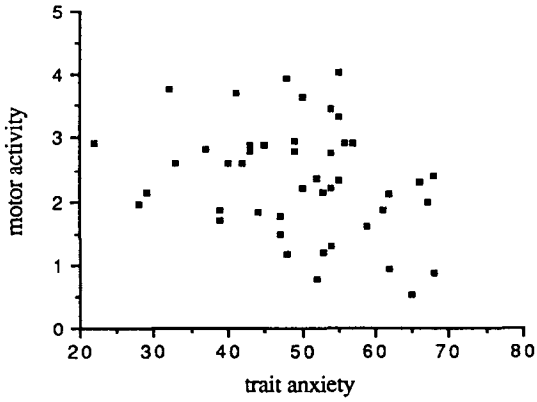
Table 3. Activity and tonic heart rate (HR) in controls and panic disorder (PD) patients categorized by degree of phobic avoidance (mean ± SD)

	Activity	Sleeping HR	Waking HR	Waking HR controlled for activity
1. Controls	2.09 ± 0.71	64.7 ± 9.1	85.5 ± 9.5	85.9 ± 9.7
2. PD without avoidance	3.04 ± 0.67	64.0 ± 6.9	88.1 ± 7.2	86.8 ± 7.5
3. PD limited avoidance	2.26 ± 0.74	66.8 ± 10.0	90.0 ± 10.7	90.1 ± 10.3
4. PD extensive avoidance	1.97 ± 1.38	65.7 ± 8.5	83.3 ± 9.7	82.4 ± 9.3
F ($df = 3, 94/3, 87/3, 98$), probability	6.0 < 0.001	0.5 NS	1.9 NS	2.9 NS
Significant comparisons (by Scheffé F test)	2 > 1, 3, 4	—	—	—

demonstrate any significant differences between the control group and the three panic disorder patient groups (females: waking HR, $F = 1.50$; $df = 3, 74$; p = NS; sleeping HR: $F = 1.11$; $df = 3, 68$; p = NS; males: waking HR: $F = 0.88$; $df = 3, 23$; p = NS; sleeping HR: $F = 2.46$; $df = 3, 21$; p = NS). BMI showed no significant correlations with activity ($r = -0.06$, $df = 86$, p = NS), waking HR ($r = 0.18$, $df = 87$, p = NS), or sleeping HR ($r = 0.15$, $df = 80$, p = NS).

With the combined sample of panic patients and control subjects, a statistically significant correlation between trait anxiety and activity was not demonstrated ($r = 0.03$; $df = 71$, p = NS). In panic disorder patients, there was a statistically significant negative correlation between trait anxiety and activity ($r = -0.31$, $df = 44$, $p < 0.05$; see Fig. 1) but not with panic attack frequency ($r = -0.22$, $df = 57$, p = NS). In control subjects, there was a positive correlation between trait anxiety

Fig. 1. Negative correlation between trait anxiety and daily activity in panic disorder patients



In panic disorder patients, there was a statistically significant negative correlation ($r = 0.31$, $p < 0.05$) between trait anxiety and mean daily activity, as illustrated in this scatterplot.

and activity which was not statistically significant ($r = 0.37$, $df = 25$, $p = 0.06$, see Fig. 2). With the combined sample, a statistically significant "inverted U" relationship between trait anxiety and activity was observed. This relationship was expressed by the following quadratic equation: Activity = -0.0015 Trait Anxiety^2 + 0.13 Trait Anxiety − 0.51. This formula accounted for a statistically significant, although relatively small, proportion of the variance in activity (multiple $r = 30$, $r^2 = 0.09$; $F = 3.58$; $df = 2, 70$; $p < 0.05$; see Fig. 3).

Trait anxiety did not show significant correlations with HR, either with the combined sample (waking HR: $r = 0.06$, $df = 70$, p = NS; sleeping HR: $r = -0.02$, $df = 64$, p = NS), controls (waking HR: $r = 0.31$, $df = 24$, p = NS; sleeping HR: $r = 0.23$, $df = 20$, p = NS), or patients (waking HR: $r = -0.06$, $df = 44$, p = NS; sleeping HR: $r = -0.03$, $df = 42$, p = NS).

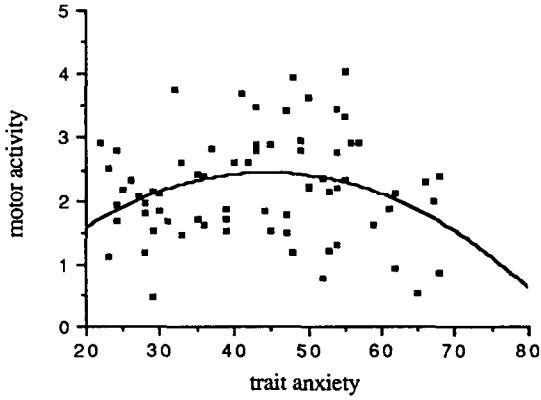
There was a significant intercorrelation between depression and activity ($r = -0.29$, $df = 57$, $p < 0.05$), as well as a difference between patient groups, on depression (see Table 2). When depression was controlled for, degree of phobic avoidance still accounted for a significant proportion of the variance in activity ($F = 6.7$, $df = 56$,

Fig. 2. Nonsignificant correlation between trait anxiety and daily activity in controls

In control subjects, the correlation ($r = 0.37, p = 0.06$) between trait anxiety and mean daily activity was not statistically significant. This scatterplot is shown in contrast to Fig. 1.

$p < 0.001$). Trait anxiety was also highly correlated with depression ($r = 0.69$, $df = 44$, $p < 0.001$). The partial correlation between trait anxiety and activity in panic disorder patients when depression was controlled for was not statistically significant ($r = 0.04$, $df = 42$, $p =$ NS).

Fig. 3. Mathematical model of relationship between trait anxiety and mean daily activity, derived from these data, superimposed on the combined patient and control samples



Discussion

Although the magnitude of the differences was relatively small, panic disorder patients without avoidance were more active than control subjects, as well as patients with limited or extensive avoidance. Controlling for depression did not negate this finding. While there was a relatively higher proportion of males in the panic disorder without avoidance group, activity did not differ between males and females, and it is

therefore unlikely that this influenced the result. The sample had similar characteristics to others reported in the literature (e.g., Ballenger et al., 1988), although there was a somewhat lower proportion of patients with extensive avoidance.

The interpretation of this result must be considered highly speculative, as motor activity is a very objective but very nonspecific variable. Clinically, the relatively high degree of activity in panic disorder patients without phobic avoidance may result from agitation or restlessness. The relatively lower activity in the panic disorder patients with agoraphobia may result from the restrictions in movement associated with avoidance or, more generally, from reductions in exploratory behavior. The intercorrelations among trait anxiety, depression, and activity in panic disorder patients suggest that a common factor, which clinically may be described as psychomotor retardation, accounts for the negative correlation of both trait anxiety and depression with activity.

The measurement of trait anxiety allowed analyses with a continuous variable across all subjects (i.e., patients and controls combined). While the nonlinear relationship with activity, expressed by a quadratic equation, was statistically significant, it accounted for only a very small proportion of the variance. Nevertheless, the presence of this relationship is of theoretical interest, as Gray and Smith (1969; Gray, 1987) have developed a mathematical model predicting a similar relationship between total appetitive behavior and aversive drive.

After medication use, activity level, and phobic elements of laboratory exposure were controlled for, HR was not significantly higher in patients than in controls. This suggests that the observation of higher resting HR in panic patients compared with controls in the laboratory is a result of anticipatory anxiety. While this does not negate the possibility that autonomic nervous system abnormalities contribute to the etiology of panic disorder, the evidence with tonic HR does not support this hypothesis.

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