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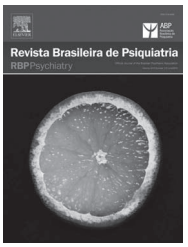

BRIEF COMMUNICATION

Cardiorespiratory response to physical exercise and psychological variables in panic disorder

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Abstract

Objective: To investigate the possible influence of psychological variables on cardiorespiratory responses and perceived exertion of patients with Panic Disorder (PD) during a submaximal exercise test. *Method*: Ten outpatients with PD and 10 matched healthy subjects walked up on a treadmill slope at a speed of 4 km/h in order to reach 65% of their maximum heart rate. Cardiorespiratory variables were continuously recorded. Before the exercise, the state and trait anxiety (State-Trait Anxiety Inventory scores), fear of physical sensations (Body Sensation Questionnaire scores), and fear of autonomic arousal (Anxiety Sensitivity Index scores) were assessed; during the exercise, levels of anxiety (VAS-A) and exertion (Borg Scale CR 10) were measured. *Results*: Compared to controls, patients reached earlier the target HR and the ventilatory threshold, showed lower oxygen consumption, higher HR and lower within-subject standard deviations of HR (a measure of cardiac variability). Exertion was also higher, and there was a significant correlation between breathing frequency, tidal volume and HR. No significant associations were found between cardiorespiratory response, perceived exertion, and psychological variables in patients with PD. *Conclusion*: Although patients with PD presented poor cardiorespiratory fitness and were required to spend more effort during physical exercise, this did not appear to be related to the psychological variables considered. Further studies with larger groups are warranted.

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DESCRITORES:
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A resposta cardiorrespiratória ao exercício e variáveis psicológicas no transtorno do pânico

Resumo
Objetivo: Investigar a possível influência de variáveis psicológicas na resposta cardiorrespiratória e percepção de esforço dos pacientes com Transtorno do Pânico (TP) durante exercício físico de intensidade submáxima. *Método*: Dez pacientes ambulatoriais com TP e dez controles saudáveis foram submetidos a uma caminhada na velocidade de 4 km/h em uma rampa inclinada. A inclinação da rampa foi aumentada até que fosse atingida 65% da frequência cardíaca máxima (FC alvo). Variáveis cardiorespiratorias foram monitoradas continuamente. Antes do exercício o *Inventário de Estado-Traço de Ansiedade*, o *Índice de Sensibilidade à Ansiedade* e o *Questionário de Sensações Corporais* foram aplicados. Durante o exercício, o nível de ansiedade (Escala Análoga Visual para Ansiedade — VAS-A) e esforço (Escala Borg CR 10) foram medidos. *Resultados*: Comparados aos controles, os pacientes atingiram a FC alvo e o limiar respiratório mais rápido, tiveram menor consumo de oxigênio, FC mais alta e menor desvio padrão da FC em cada sujeito (medida de variabilidade cardíaca). O esforço também foi maior e houve uma correlação significativa entre frequência respiratória, volume corrente e FC. Nenhuma associação significativa foi encontrada entre cardiorrespiratória resposta, percepção de esforço e variáveis psicológicas em pacientes com TP. *Conclusão*: Pacientes com TP mostrou baixa aptidão cardiorrespiratória e maior esforço durante o exercício físico que não pareceu estar relacionada com as variáveis psicológicas consideradas. Mais estudos em grupos maiores são necessários.

Introduction

Several studies showed that patients with Panic Disorder (PD) have a poor cardiovascular fitness conditioning and low exercise tolerance.[1-3] The extent to which their poorer aerobic performances may be related to the actual function of their cardio-respiratory system or affected by psychological variables, such as anxiety levels during fitness testing or catastrophic misinterpretation of physical symptoms has not, however, been satisfactorily clarified; one study showed that high anxiety sensitivity may partly contribute to poor cardiovascular fitness estimation and exercise intolerance in patients with PD.[3] Thus, to evaluate the influence of psychological variables on fitness estimation assessment of patients with PD, we investigated the possible association between their cardiorespiratory response and perceived exertion during submaximal exercise, as well as their state anxiety both before and during exercising, trait anxiety, fear of physical sensations, and fear of autonomic arousal.

Method

Ten outpatients with Panic Disorder (PD), 8 with agoraphobia and 2 without, and 10 healthy subjects with no lifetime psychiatric disorders[4] were included in the study. Exclusion criteria were lifetime cardio-circulatory, respiratory and endocrine diseases, hypertension (systolic pressure > 140 mmHg, diastolic > 90 mmHg), pregnancy or epilepsy, and Body Mass Index > 24.9 or < 18.5. Both groups were matched for age and gender (patients: 6 women and 4 men, mean age 36.1 years, SD 8.7 years; controls: 6 women and 4 men, mean age 36.6 years, SD 7.0 years), smoking habit, and practicing a sport activity: one man and one women from each group were smokers (3 to 5 cigarettes/day); the other subjects had never smoked any cigarettes/other tobacco products. One man from each group had been swimming 1 hour/week during the preceding 6 months; the other subjects had not engaged in any kind of sports activity in the year before recruitment.

Subjects had been free from psychotropic medications for at least 2 weeks before the evaluation; alcohol for at least 36 hours; xanthines for at least 8 hours; smoking for at least 2 hours; had consumed a light lunch up to 3 hours before the exercise test, which took place between 4 p.m. and 6 p.m. This study was approved by the Ethics Committee *Azienda Sanitaria Lo*cale (ASL), city of Milan, and written informed consents were obtained from the subjects.

The submaximal exercise test consisted of a 4 km/h walk on a treadmill with an increasingly steeper slope to reach 65% of the maximum heart rate (target HR), calculated using Karvonen's formula, considering both rest HR and age of each subject.[5] The exercise test included the following phases: 1) three minutes standing on the treadmill without walking, 2) three minutes walking on a 0% slope (warm-up), 3) walking up on an increasingly steeper slope (3% every two minutes) up to 65% of the maximum HR, 4) three minutes walking up a slope to the point where the subject reached his/her target HR (maximum slope), maintaining a HR between 65% and 75% of the maximum HR (maintenance), 5-8) subsequent recovery-phases: two minutes walking up a slope half the maximum slope, two minutes walking on a 0% slope, followed by two minutes standing on the treadmill without walking, and two minutes sitting down.

The exercise test was interrupted in case the HR exceeded 75% of the maximum HR. In each phase of the session, subjects quantified the level of effort spent based on the Borg Scale CR 10[6] and their anxiety level using the Visual Analogue Scale for Anxiety (VAS-A) (Table 1). Before

instructing subjects about the evaluation, baseline anxiety was assessed according to the State-Trait Anxiety Inventory for state anxiety.[7]

Throughout the entire test, heart rate and respiratory variables were recorded on a breath by breath basis using a thoracic band and a face mask, based on the Quark b2 stationary testing system (Cosmed, Rome, Italy) following the recommendations of the American Thoracic and European Respiratory Societies.

The following variables were recorded: heart rate (beats/minute), breathing frequency (breaths/minute), tidal volume (liter), minute ventilation (liters/minute), time of inspiration and expiration (seconds), inspiratory length to total breath length ratio, carbon dioxide output (V_{CO2}, mL/minute), oxygen uptake (V_{O2}, mL/minute), end-tidal carbon dioxide partial pressure (mmHg), oxygen consumption (mL/kg/minute), and peak of oxygen consumption and ventilatory threshold estimated by the gas exchange criterion of an increase in V_{CO2} relative to V_{O2} ("V-slope" technique).

The severity of clinical symptoms of patients with PD was measured using the Panic Associated Symptoms Scale.[8] The following variables were measured for each subject: trait anxiety (State-Trait Anxiety Inventory[7]), fear of physical sensations (Body Sensations Questionnaire[9]), and fear of autonomic arousal (Anxiety Sensitivity Index[10]).

Non-parametric statistical tests, including the Mann-Whitney U Test, Friedman Test, and Spearman correlation were performed. Categorical variables were analysed using Fisher's Exact Test (Statistica 5.5 software system, Statsoft).

Results

Cardiorespiratory variables and exertion

Patients and controls did not differ in terms of resting and target heart rate (Table 1). Patients achieved the target heart rate on a flatter slope than controls (11.7, SD 4.6 vs. 17.1, SD 3.5, Z = -2.45, p < 0.05). Patients showed significantly higher heart rates than controls in six phases of the workout session (Table 1) and a significantly lower average within-subject standard deviations (SDs) of heart rate in two of the session´s phases, namely at recovery at half of the maximum slope (4.2, SD 2.1 vs. 7.5, SD 1.9, Z = -2.69, p < 0.01) and at 0% slope (4.1, SD 1.7 vs. 5.7, SD 1.4, Z = -2.28, p < 0.05).

Patients had a lower oxygen consumption than controls at the target heart rate (25.1, SD 4.3 vs. 29.8, SD 2.9, Z = -2.42, p < 0.05), and a lower peak of oxygen consumption during the maintenance phase (28.3, SD 3.9 vs. 35.1, SD 4.6, Z = -2.79, p < 0.01). Nine patients (90%) and 4 controls (40%) achieved the ventilatory threshold when on the 9% slope, whereas 1 patient (10%) and 6 controls (60%) achieved it between the 12% slope and the recovery phase on the 0% slope (p < 0.05).

Patients and controls did not significantly differ in terms of mean and SDs values regarding all the other respiratory variables.

Patients, unlike controls, showed significant correlations between heart rate and breathing frequency in five phases (standing (R = 0.73, p < 0.05), warm-up (R = 0.81, p < 0.01), 3% slope (R = 0.65, p < 0.05), 9% slope (R = 0.76, p < 0.05), 12% slope (R = 0.82, p < 0.05)), and between heart rate and tidal volume in four phases (half of the maximum slope (R = -0.75, p < 0.05), recovery at 0% slope (R = -0.71, p < 0.05), standing recovery (R = -0.82, p < 0.01), and sitting recovery (R = -0.76, p < 0.05).

A significant change in effort levels over the workout was seen in both patients (df = 6; Chi-Square = 44,9; p < 0.0001) and controls (df = 6, Chi-Square = 44,63; p < 0.0001); patients reported exerting more effort than controls in the warm-up phase and at the target heart rate (Table 1). One patient interrupted the exercise during the maintenance phase due to exhaustion and, in one particular case, the maintenance phase had to be shortened because the patient´s resting heart rate had exceeded 75%.

Psychological variables

Patients experienced higher anxiety levels than controls at all the phases of the exercise test (Table 1), although these levels fell significantly as the test progressed (df = 7, Chi-Square = 25,74; p < 0.001); controls did not show significant changes in anxiety levels throughout the exercise. Compared to controls, patients scored higher in the psychometric scales (Table 1).

In both groups, no correlations were found between evaluation-related anxiety levels, psychometric scale scores and exertion, heart rate, or respiratory variables during the entire evaluation. None of the psychometric scores or procedural anxiety levels of patients who achieved the target heart rate when the slope was set below 12% (n = 7) differ from those of the subjects who achieved the target heart rate when the slope was above 12% (n = 3).

During the exercise test, no patient experienced any panic attacks.

Discussion

Patients with PD showed a poorer cardiorespiratory response, diminished tolerance, and a stronger perception of exertion during physical exercise than the controls matched for individual variables and sport activity. Patients reached the target HR and the ventilatory threshold earlier than controls, and showed a lower oxygen consumption during the most exhausting phases of the exercise. In the recovery phases, they showed a higher HR and a lower SDs of HR, indicating lower cardiac variability; finally, a significant correlation was found in patients between breathing frequency, tidal volume, and HR in certain phases of the exercise, while this was not the case for controls.

We did not find significant associations between cardio-respiratory response, perceived exertion, and psychological variables in patients with PD. In alignment with previous findings about the anxiolytic effect of acute exercise in patients with PD,[11] and although anxiety levels during exercising were higher in patients than in controls, these levels significantly decreased during the evaluation, and did not correlate with exertion, heart rate or respiratory variables in any phase of the exercise. Similarly, state anxiety before the evaluation, trait anxiety, fear of physical sensations, and fear of autonomic arousal correlated neither with perceived effort nor with cardio-respiratory variables. Last but not least, the patients who achieved the target heart rate on flatter slopes did not differ from those who achieved the target heart rate on steeper slopes, either in terms of the disease severity or in any of the psychological variables considered.

Considering the small size of our sample, our results have confirmed previous findings on the poor fitness condition of

Table 1 Heart rate, anxiety, and subjective exertion during the procedure; psychological variables

	Patients with PD (n = 10)	Healthy subjects (n = 10)	Z	p†
Rest HR	81.9 (9.4) (n = 10)	75.2 (9.2) (n = 10)	1.66	0.1
Target HR	148.8 (8.9) (n = 10)	145.1 (5.2) (n = 10)	0.90	0.4
Standing HR	91.6 (7.5) (n = 10)	87.0 (9.2) (n = 10)	1.38	0.2
Warm-up HR	112.7 (9.7) (n = 10)	98.6 (9.1) (n = 10)	2.53	< 0.05
HR 3%	117.5 (11.2) (n = 10)	103.9 (7.5) (n = 10)	2.64	< 0.01
HR 6%	127.6 (12.8) (n = 10)	112.3 (9.4) (n = 10)	2.64	< 0.01
HR 9%	134.4 (12.9) (n = 8)	120.4 (10.8) (n = 10)	2.57	< 0.01
HR 12%	137.2 (12.1) (n = 6)	129.0 (12.2) (n = 10)	1.62	0.1
HR 15%	130.4 (3.8) (n = 3)	132.5 (6.1) (n = 8)	-0.41	0.7
HR 18%	135.2 (n = 1)	139.1 (5.9) (n = 6)	-	-
HR 21%	142.5 (n = 1)	140.0 (3.7) (n = 3)	-	-
M HR	150.2 (11.3) (n = 10)	148.1 (6.0) (n = 10)	0.30	0.8
HS HR	145.1 (11.5) (n = 9)	139.3 (8.9) (n = 10)	1.14	0.3
HR recovery 0%	131.6 (12.3) (n = 9)	120.5 (9.2) (n = 10)	2.12	< 0.05
Standing recovery HR	117.1 (10.4) (n = 9)	108.5 (10.2) (n = 10)	1.22	0.2
Sitting recovery HR	102.1 (9.0) (n = 9)	92.8 (7.4) (n = 10)	2.04	< 0.05
STAI-T	49.4 (13.2)	34.5 (5.3)	2.6	< 0.05
ASI	30.3 (8.9)	9.2 (6.6)	3.6	< 0.001
BSQ	3.1 (1.1)	1.5 (0.4)	3.6	< 0.001
STAI-S	45.4 (11.6)	28.9 (3.7)	3.5	< 0.001
VAS-A Pre-exercise	47.6 (22.2)	1.4 (3.3)	3.32	< 0.001
VAS-A Standing	38.4 (21.8)	2.2 (3.9)	3.28	< 0.01
VAS-A Warm-up	37.7 (23.2	1.4 (2.9)	3.28	< 0.01
VAS-A Target heart rate	34.2 (24.5)	7.2 (12.6)	2.64	< 0.01
VAS-A Maintenance	35.9 (26.9)	10.6 (14.5)	2.41	< 0.05
VAS-A Recovery 0% slope	22.1 (22.4)	1.1 (1.8)	2.57	< 0.05
VAS-A Standing recovery	22.5 (25.4	2.0 (4.8)	2.44	< 0.05
VAS-A Sitting recovery	11.7 (13.6)	0.8 (2.5)	2.69	< 0.01
Borg Standing	0.2 (0.3)	0.06 (0.1)	0.52	0.5
Borg Warm up	1.6 (1.7)	0.2 (0.2)	3.32	< 0.001
Borg Target heart rate	4.2 (2.1)	1.7 (1.5)	2.65	< 0.01
Borg Maintenance	5.0 (2.2)	3.4 (2.2)	1.09	0.3
Borg Recovery 0% slope	1.6 (1.2)	0.7 (0.7)	1.79	0.07
Borg Standing recovery	0.8 (1.8)	0.4 (0.7)	1.02	0.3
Borg Sitting recovery	0.3 (0.4)	0.03 (0.1)	1.34	0.2

Values are expressed as mean (SD); HR: Heart rate (beats/minute); HR 3%-21%: Heart rate at the different increasing slopes; M HR: Heart rate at half maintenance phase (between 65% and 75% of rest HR); HS HR: Heart rate at half of the maximum slope; HR recovery 0%: Heart rate at 0% slope; STAI-T: State-Trait Anxiety Inventory for Trait Anxiety (before the procedure instructions); STAI-S: State Trait Anxiety Inventory for State Anxiety (before the procedure instructions); ASI: Anxiety Sensitivity Index; BSQ: Body Sensations Questionnaire; VAS-A: Visual Analogue Scale for Anxiety, describing the global subjective anxiety on a continuum from 0 (no anxiety) to 100 (the worst anxiety imaginable); VAS-A pre-exercise: after the procedure instructions, before going up the treadmill; Borg: Borg Scale CR 10 (range 0-10); n: number of subject in each phase; †: U Mann-Whitney test.

patients with PD[1-3] and, in parallel, previous results of their abnormal cardiorespiratory function, including sensation of "respiratory effort",[12] decreased heart-rate variability,[13] and malfunction of autonomic system.[13] Moreover, we found that their poor cardiorespiratory response and low exercise tolerance did not appear to be related to anxiety levels before or during exercise, trait anxiety, fear of physical sensations, or fear of autonomic arousal. This suggests that the poor fitness condition of patients with PD might be related to an actual malfunction of their cardiorespiratory system, causing patients to be less able to cope with physical perturbations; this may be partly due to the pathophysiology of PD and contribute to the cardiovascular morbidity of PD patients.[13] However, other possible explanations may account for our results. First, the sample size was very small, limiting the study´s power to show significant associations and, although patients and controls were matched for sport activities, it is possible that the poorer fitness conditioning seen in patients with PD might be related to avoidance behaviours and reduced outdoors activities. Second, although patients had been not taken any psychotropic medications for at least 2 weeks before the evaluation, we cannot completely exclude the influence of previous therapies on their cardiorespiratory responses. Finally, we cannot exclude that interoceptive conditioned responses or emotional reactions to physical symptoms during exercise may have influenced our results, as they may have gone undetected due to the psychometric scales used.

Conclusions

Compared to controls, patients with PD showed poorer cardiorespiratory responses and a stronger perception of exertion during physical exercise; both of which did not appear to be associated with the psychological variables under study. Because the sample size was very small and the fact that several other explanations for our findings are possible, further studies with larger groups are warranted.

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Disclosures

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* Modest
** Significant
*** Significant: Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.

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