



apunts

MEDICINA DE L'ESPORT

[www.apunts.org](http://www.apunts.org)



## ORIGINAL ARTICLE

# Respiratory response to low-intensity physical exercise in women with chronic fatigue syndrome

Elisabet Guillaumò<sup>a</sup>, Alicia Blazquez<sup>a</sup>, Agustí Comella<sup>b</sup>, Rubén Martínez-Rodríguez<sup>a,c</sup>, Eduardo Garrido<sup>d</sup>, Joan Ramon Barbany<sup>a</sup>, Josep Lluís Ventura<sup>a,e</sup> and Casimiro Javierre<sup>a,\*</sup>

<sup>a</sup>Physiology Unit, Department of Physiological Sciences II, Faculty of Medicine, University of Barcelona, Barcelona, Spain

<sup>b</sup>Exercise Physiology Unit, Hospital General de Catalunya, Sant Cugat del Vallès, Barcelona, Spain

<sup>c</sup>Anesthesiology Unit, University Hospital of Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

<sup>d</sup>Sciences and Social Sciences Department, University of Vic, Vic, Barcelona, Spain

<sup>e</sup>Critical Care Unit, University Hospital of Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

Received on December 30, 2009; accepted on January 12, 2010

### KEYWORDS

Chronic fatigue syndrome;  
Exercise;  
Physiological response

### Abstract

**Introduction:** The aim of the study was to evaluate the cardiorespiratory parameters at rest and as the response to very low intensity physical exercise in women with chronic fatigue syndrome (CFS).

**Material and methods:** A group of 141 women suffering from CFS were compared with a control group (C) of 20 women while at rest and during 4 minutes of constant exercise on a cycloergometer with no work load (work load = 0 watts).

**Results:** Significant differences were found during the exercise: respiratory quotient (CFS =  $0.9 \pm 0.09$ ; C =  $0.8 \pm 0.08$ ;  $p < 0.05$ ); the respiratory equivalent for oxygen (CFS =  $34.6 \pm 10.1$ ; C =  $28.0 \pm 3.4$ ;  $p < 0.01$ ) and for carbon dioxide (CFS =  $37.9 \pm 7.7$ ; C =  $33.4 \pm 3.8$ ;  $p = 0.01$ ). Differences were observed in the heart rate during the rest period (CFS =  $86.8 \pm 14.2$  beats·min<sup>-1</sup>; C =  $79.8 \pm 8.4$  beats·min<sup>-1</sup>;  $p = 0.03$ ). There were no significant differences in the perception of effort made during rest (CFS =  $10.3 \pm 3.0$ ; C =  $6.2 \pm 0.6$ ;  $p < 0.001$ ) and just after exercise (CFS =  $12.5 \pm 2.8$ ; C =  $6.8 \pm 1.4$ ;  $p < 0.01$ ).

**Conclusions:** It was concluded that women with chronic fatigue syndrome had less ventilatory efficiency than the controls during low intensity physical exercise. This condition could be improved through specific rehabilitation programs.

© 2009 Consell Català de l'Esport. Generalitat de Catalunya. Published by Elsevier España, S.L. All rights reserved.

\*Corresponding author

E-mail: [cjavierre@ub.edu](mailto:cjavierre@ub.edu) (C. Javierre).

**PALABRAS CLAVE**

Síndrome de fatiga crónica;  
Ejercicio;  
Respuesta fisiológica

**Respuesta respiratoria al ejercicio físico de baja intensidad en mujeres con síndrome de fatiga crónica****Resumen**

**Introducción:** El objetivo del estudio fue evaluar los parámetros cardiorrespiratorios en condiciones de reposo y la respuesta durante el ejercicio físico a muy baja intensidad en mujeres con síndrome de fatiga crónica (SFC).

**Material y métodos:** Un grupo de 141 mujeres afectadas por el SFC se compararon con un grupo control (C) de 20 mujeres en condiciones de reposo y durante 4 min de ejercicio constante en un cicloergómetro sin carga de trabajo (carga de trabajo = 0 vatios).

**Resultados:** Se encontraron diferencias significativas durante el ejercicio: el cociente respiratorio (SFC =  $0,9 \pm 0,09$ ; C =  $0,8 \pm 0,08$ ;  $p < 0,05$ ); equivalente respiratorio para el oxígeno (SFC =  $34,6 \pm 10,1$ ; C =  $28,0 \pm 3,4$ ;  $p < 0,01$ ) y para el dióxido de carbono (SFC =  $37,9 \pm 7,7$ ; C =  $33,4 \pm 3,8$ ;  $p = 0,01$ ). Se observaron diferencias en la frecuencia cardíaca durante el período de descanso (SFC =  $86,8 \pm 14,2$  latidos·min<sup>-1</sup>; C =  $79,8 \pm 8,4$  latidos·min<sup>-1</sup>;  $p = 0,03$ ). No hubo diferencias significativas en la percepción del esfuerzo realizado durante el descanso (SFC =  $10,3 \pm 3,0$ ; C =  $6,2 \pm 0,6$ ;  $p < 0,001$ ) y justo después del ejercicio (SFC =  $12,5 \pm 2,8$ ; C =  $6,8 \pm 1,4$ ;  $p < 0,01$ ).

**Conclusiones:** Se concluye que las mujeres con síndrome de fatiga crónica tenían menos eficiencia ventilatoria que los controles durante el esfuerzo físico a baja intensidad. Este aspecto podría ser mejorado mediante programas específicos de rehabilitación.

© 2009 Consell Català de l'Esport. Generalitat de Catalunya. Publicado por Elsevier España, S.L. Todos los derechos reservados.

**Introduction**

One of the main characteristics of patients affected by chronic fatigue syndrome (CFS) is their reduced exercise capacity and increased fatigue symptoms. CFS patients have a marked ratio of perceived exertion (RPE) hours and even days after physical effort<sup>1</sup>. Several studies have reported a reduction in aerobic power in CSF patients, with low values of maximal oxygen uptake ( $VO_{2peak}$ ), heart rate, and workload<sup>2-4</sup>. Patients with CFS had a higher RPE at the beginning of physical exercise, during submaximal and peak workloads, and during recovery time<sup>5</sup>. Most of the research has assessed the functional capacity of these patients using incremental protocol test methods. The aim of these tests is to obtain the maximum cardiorespiratory values. However, there are no studies of the cardiorespiratory response in CFS during light exercise, which could represent CSF patients' daily activities.

Therefore, we assessed some physiological parameters in CSF patients during rest and during very low intensity, steady state physical exercise.

**Methods**

A group of 141 women affected by CFS (age:  $46.7 \pm 8.7$  years; height:  $160.4 \pm 0.6$  cm; weight:  $67.1 \pm 13.2$  kg) were compared with a control group (C) of 20 women (age:  $42.9 \pm 11$  years;

height:  $158.9 \pm 6.4$  cm; weight:  $66.7 \pm 10.9$  kg) with similar social and activity levels. The study was approved by the Ethical Committee (IDIBELL. Campus od Bellvitge). All subjects signed the corresponding consent form. Patients were carefully assessed to check that they met CDC (Centre for Disease Control) criteria for CFS. Previous diagnoses were confirmed by the consensus of two specialists.

**Laboratory Tests**

All tests were performed in the endurance laboratory of the Department of Physiological Sciences II (IDIBELL-University of Barcelona. Campus of Bellvitge). Environmental parameters were stable and optimum throughout the tests (temperature: 22-24 °C; relative humidity: 55-66%). Participants did not perform any kind of high-intensity physical activities in the 72 hours previous to the test and all stated that they had slept normally the night before. The tests were conducted in the morning after a light breakfast with no stimulant or depressant beverages. Subjects were evaluated while resting for 2 minutes on the cycloergometer (Excalibur, Lode, Groningen, Netherlands). Then, they cycled with no workload (0 watts) at 50 rpm for 4 minutes. This exercise time is sufficient to achieve a steady state in heart rate, ventilation, oxygen and carbon dioxide kinetics, particularly during a test with no workload. A breath-by-breath automatic system (Metasys TR-plus, Brainware

S.A., La Valette, France) measured airflow and volume continuously and simultaneously determined expired carbon dioxide ( $\text{VCO}_2$ ) and oxygen uptake ( $\text{VO}_2$ ) using a two-way mask (Hans Rudolph, Kansas, USA). Heart rate (HR) was monitored continuously by means of a pulsometer (Polar Acurex Plus, Polar Electro OY, Finland) and blood pressure was recorded at the end of both the rest and exercise phases. Age-based, predicted values of  $\text{VO}_{2\text{max}}$  were calculated from regression equations derived from maximal testing in a cohort of healthy sedentary women ( $\text{VO}_{2\text{max}}$  in  $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1} = 42.3 - [0.356\cdot\text{age in years}]^6$ ).

The RPE was determined using the Borg Scale<sup>7</sup> during resting and just after the exercise period. Ventilation (VE),

$\text{VO}_2$ ,  $\text{VCO}_2$  and HR data were averaged for the whole rest period and for the last 2 minutes of the exercise period.

## Statistical Analysis

The Kolmogorov-Smirnov test was used to determine the normal distribution of the different variables. The differences between the values recorded in the C and CFS groups were analysed by Student's t test for unpaired samples. The significance level was  $p < 0.05$  for all the statistical variables.

## Results

There were no significant differences in the physical or functional characteristics of the subjects studied (Table 1).

There were no significant differences in the resting ventilatory values between both groups. However, the HR (mean  $\pm$  SD) was significantly higher ( $p = 0.03$ ) in CFS patients (CFS =  $86.8 \pm 14.2$   $\text{beat}\cdot\text{min}^{-1}$ ; C =  $79.8 \pm 8.4$   $\text{beat}\cdot\text{min}^{-1}$ ), as was the RPE scale (CFS:  $10.3 \pm 3$ ; C:  $6.2 \pm 0.6$ ;  $p < 0.001$ ).

During exercise, ventilatory differences were detected between both groups in the respiratory equivalents of  $\text{VO}_2$  (CFS =  $34.6 \pm 10.1$ ; C =  $28 \pm 3.4$ ;  $p < 0.01$ ) and  $\text{VCO}_2$  (CFS =  $37.9 \pm 7.7$ ; C =  $33.4 \pm 3.8$ ;  $p = 0.01$ ). We also found

**Table 1** The characteristics of both groups

	CFS group	Control group
Age (years)	$46.7 \pm 8.7$	$42.9 \pm 11.0$
Weight (kg)	$67.1 \pm 13.2$	$66.7 \pm 10.9$
Height (cm)	$160.4 \pm 0.6$	$158.9 \pm 6.4$
$\text{VO}_2$ theoretical max ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	$25.7 \pm 3.3$	$27.0 \pm 3.9$
HR theoretical max ( $\text{beats}\cdot\text{min}^{-1}$ )	$173.8 \pm 8.8$	$177.7 \pm 10.9$
Work Power theoretical max (w)	$131.5 \pm 21.8$	$136.6 \pm 18.7$

CFS: chronic fatigue syndrome, HR: Heart Rate,  $\text{VO}_2$ : Oxygen consumption.

**Table 2** Physiological parameters during rest and cycling with no workload (0 watts) in the chronic fatigue syndrome (CFS) and control groups

Parameters	Rest		0 watts	
	CFS group	Control group	CFS group	Control group
$\text{V}_E$ ( $\text{L}\cdot\text{min}^{-1}$ )	$10.4 \pm 2.9$	$9.57 \pm 1.8$	$19.6 \pm 7.3$	$16.0 \pm 2.6$
$\text{B}_T$ ( $\text{breaths}\cdot\text{min}^{-1}$ )	$17.8 \pm 4.1$	$17.0 \pm 4.0$	$23.3 \pm 6.5$	$21.7 \pm 4.2$
$\text{V}_T$ (L)	$0.5 \pm 0.1$	$0.5 \pm 0.0$	$0.7 \pm 0.2$	$0.6 \pm 0.1$
$\text{VO}_2$ ( $\text{L}\cdot\text{min}^{-1}$ )	$0.3 \pm 0.0$	$0.3 \pm 0.0$	$0.5 \pm 0.1$	$0.5 \pm 0.1$
$\text{VO}_2$ ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	$5.0 \pm 1.4$	$4.7 \pm 1.0$	$8.6 \pm 2.4$	$8.7 \pm 1.7$
RER	$0.8 \pm 0.0$	$0.8 \pm 0.0$	$0.9 \pm 0.1$	$0.8 \pm 0.0^*$
$\text{FEO}_2$ (%)	$17.0 \pm 0.6$	$16.9 \pm 0.4$	$17.2 \pm 0.7$	$16.6 \pm 0.4^*$
$\text{FECO}_2$ (%)	$3.2 \pm 0.5$	$3.2 \pm 0.3$	$3.3 \pm 0.5$	$3.6 \pm 0.3^*$
$\text{V}_E/\text{VO}_2$ (L)	$32.2 \pm 6.4$	$30.9 \pm 4.7$	$34.6 \pm 10.1$	$28.0 \pm 3.4^*$
$\text{V}_E/\text{VCO}_2$ (L)	$39.0 \pm 7.5$	$38.1 \pm 4.0$	$37.9 \pm 7.7$	$33.4 \pm 3.3^*$
PET $\text{O}_2$ (mmHg)	$107.0 \pm 5.7$	$105.4 \pm 4.9$	$109.2 \pm 7.5$	$103.2 \pm 3.8^*$
PET $\text{CO}_2$ (mmHg)	$34.6 \pm 4.6$	$35.0 \pm 3.2$	$34.4 \pm 5.9$	$37.9 \pm 3.2^*$
HR ( $\text{beats}\cdot\text{min}^{-1}$ )	$86.8 \pm 14.2$	$79.8 \pm 8.4^*$	$101.4 \pm 7.9$	$96.3 \pm 7.3$
Systolic BP (mmHg)	$124.01 \pm 17.7$	$124.45 \pm 19.4$	$132.3 \pm 20.6$	$132.9 \pm 16.1$
Diastolic BP (mmHg)	$79.09 \pm 12.4$	$76.9 \pm 8.8$	$85.0 \pm 15.6$	$93.5 \pm 13.0^{**}$
RPE	$10.0 \pm 3.0$	$6.2 \pm 0.6^{**}$	$12.5 \pm 2.8$	$6.8 \pm 1.4^{**}$

$\text{V}_E$ : minute ventilation;  $\text{B}_T$ : breathing frequency;  $\text{V}_T$ : tidal volume;  $\text{VO}_2$ : oxygen uptake; RER: respiratory exchange ratio;  $\text{FEO}_2$ : expiratory fraction of  $\text{O}_2$ ;  $\text{FECO}_2$ : expiratory fraction of  $\text{CO}_2$ ;  $\text{V}_E/\text{VO}_2$ : ventilatory equivalent for oxygen;  $\text{V}_E/\text{VCO}_2$ : ventilatory equivalent for  $\text{CO}_2$ ; PET  $\text{O}_2$ : end-tidal  $\text{PO}_2$ ; PET  $\text{CO}_2$ : end-tidal  $\text{PCO}_2$ ; HR: heart rate; Diastolic BP: diastolic blood pressure; Systolic BP: systolic blood pressure; RPE: rating of perceived exertion.

\* $p < 0.05$ ; \*\* $p < 0.01$ .

differences ( $p < 0.05$ ) in end-tidal pressures of oxygen ( $CFS = 109.2 \pm 7.5$  mmHg;  $C = 103.2 \pm 3.8$  mmHg) and carbon dioxide ( $CFS = 34.4 \pm 5.9$  mmHg;  $C = 37.9 \pm 3.2$  mmHg). Likewise, differences ( $p < 0.05$ ) were detected in the respiratory quotient during exercise ( $CFS = 0.9 \pm 0.09$ ;  $C = 0.8 \pm 0.08$ ) (Table 2).

## Discussion

This study found substantial differences between women with CFS and a healthy sedentary control group after physical exercise, even at very low workloads. To avoid age, weight and activity level related influences, the selected patients had the same characteristics as the control group. There were no differences between the groups in the estimated  $VO_2$ , HR and work power peaks. This study had a larger sample than other studies that have evaluated cardiorespiratory function during submaximal exercise<sup>5</sup>.

When resting, HR was 9% higher in CFS patients. This could be explained by the following: a) a higher level of anxiety; b) autonomic system dysfunction with a sympathetic overactivity<sup>8</sup> or decreased vagal tone<sup>9</sup>, and c) smaller left systolic and diastolic ventricular dimensions and mass<sup>10</sup>, which would produce an increased HR to maintain cardiac output. Although we did not detect significant differences in resting blood pressure between both groups, the diastolic values in CFS patients were slightly higher. This suggests that CSF patients may have decreased vagal tone.

CFS patients showed a markedly worse response than controls during exercise with no added workload. In particular, CSF patients had higher respiratory equivalents for oxygen and carbon dioxide, leading to lower ventilatory efficiency than control subjects, who had 24% higher ventilation for the same  $VO_2$  uptake. In addition, we observed a higher percentage of oxygen; a higher end-tidal pressure of oxygen; a lower percentage of carbon dioxide; and lower carbon dioxide end-tidal pressures. This suggests that the alveolar pressure of both gases was probably secondary to a certain hyperventilation state. The differences in ventilation efficiency, evaluated by the respiratory equivalents for oxygen and carbon dioxide, could be explained by weaker thoracic muscles producing shallow breathing in CSF patients. It could also be linked to hyperventilation from anxiety caused by protocol procedures used in the laboratory. We evaluated ventilation during the final exercise phase and during the previous period to assess whether exercise decreased anxiety. The kinetics of these parameters could also be related to the patients' symptoms. CSF patients stated that they had a sensation of dyspnoea during the very light physical effort. The sensation of dyspnoea could increase anxiety and affect the respiratory response during exercise.

Finally, these findings could be due to reduced oxidative metabolism by muscle cells<sup>11</sup> or an altered ability to get oxygen into small muscle vessels, related to abnormal

control of peripheral circulation<sup>12</sup>. Physical inactivity causes a decrease in oxygen delivery and in the oxidative capacity of tissues. The CFS group had a significantly higher respiratory quotient. This indicates that they used a higher percentage of glucose fuels to perform the same work by mainly aerobic metabolism, as the value was less than the unit.

## Conclusion

According to our results, women with CFS had markedly less ventilatory efficiency than controls during periods of very low physical effort. Efficiency could be improved by means of rehabilitation programs, which would have great psychophysical benefits on CSF patients' daily activities.

## Conflict of interest

The authors declare they have no conflicts of interest.

## Financing

This study was funded partially by grant FIS PI051487-2006.

## Acknowledgments

We thank the clinical advice of doctors Alegre and García-Quintana.

## References

1. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med.* 1994;121:953-9.
2. De Becker P, Reynders M, McGregor N, De Meirleir K. Exercise capacity in chronic fatigue syndrome. *Arch Intern Med.* 2000;160:3270-7.
3. Javierre C, Alegre J, Ventura JL, García-Quintana, Segura R, Suárez A, et al. Physiological responses to arm and leg exercise in women patients with chronic fatigue syndrome. *JCFS.* 2007;14:43-53.
4. Nijs J, De Meirleir K. Prediction of peak oxygen in patients fulfilling the 1994 CDC criteria for chronic fatigue syndrome. *Clin Rehab.* 2004;18:785-92.
5. Wallman KE, Morton AR, Goodman C, Grove R. Physiological responses during a submaximal cycle test in chronic fatigue syndrome. *Med Sci Sports Exerc.* 2004;36:1682-8.
6. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and normographic assessment of functional aerobic in cardiovascular disease. *Am Heart J.* 1973;85:546-62.
7. Borg G. Borg's perceived exertion and pain scales. Champaign, IL: Human Kinetics; 1998.
8. Pagani M, Lucini D, Mela G, Langewitz W, Malliani A. Sympathetic overactivity in subjects complaining of unexplained fatigue. *Clin Sci.* 1994;87, 655-61.

9. Cordero D, Sisto S, Tapp W, LaManca J, Pareja J, Natelson B. Decreased vagal power during treadmill walking in patients with chronic fatigue syndrome. *Clin Auton Res*. 1996;6:329-33.
10. De Lorenzo F, Xiao H, Mukherjee M, Harcup J, Suleiman S, Kadziola Z, et al. Chronic fatigue syndrome: physical and cardiovascular deconditioning. *QJM*. 1998;91:475-81.
11. McCully K, Natelson B, Iotti S, Sisto S, Leigh J. Reduced oxidative muscle metabolism in chronic fatigue syndrome. *Muscle Nerve*. 1996;19:621-5.
12. Wilke W, Fouad-Tarazi F, Cash J, Calibrese L. The connection between chronic fatigue syndrome and neurally mediated hypotension. *Cleveland Clin J Med*. 1998;65:261-6.