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Impact of a maximal exercise test on symptoms and activity in chronic fatigue syndrome

Ellen Bazelmans[a,*], Gijs Bleijenberg[b,1], Marinus J.M. Voeten[c,2], Jos W.M. van der Meer[d,3], Hans Folgering[e,4]

[a]Department of Medical Psychology, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands
[b]Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands
[c]Department of Educational Sciences, Radboud University Nijmegen, P.O. Box 9104, 6500 HE Nijmegen, The Netherlands
[d]Department of General Internal Medicine, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands
[e]Department of Pulmonology Dekkerswald, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands

Abstract

Objective: This study examined the effects of exercise on symptoms and activity in chronic fatigue syndrome (CFS). **Methods:** Twenty CFS patients and 20 neighborhood controls performed an incremental exercise test until exhaustion. Fatigue, muscle pain, minutes spent resting, and the level of physical activity were assessed with a self-observation list. Physical activity was assessed with an actometer as well. Data were obtained 3 days before the maximal exercise test (MET) up to 5 days thereafter. **Results:** For CFS patients, daily observed fatigue was increased up to 2 days after the exercise test. For controls, self-observed fatigue returned to baseline after 2 h. Both CFS patients and controls spent more minutes resting on the day before and on the day after the MET. For CFS patients, self-observed minutes resting increased on the day of the exercise test. For neither group, a decrease of actometer recorded or self-observed physical activity after exercise was found. **Conclusion:** Fatigue in CFS patients increased after exercise, but the level of actual physical activity remained unchanged.

Keywords: Chronic fatigue syndrome; Maximal exercise test; Impact

Introduction

Chronic fatigue syndrome (CFS) is characterized by a severe, disabling, and unexplained fatigue, lasting for at least 6 months. CFS patients often report that even minimal exercise aggravates symptoms and leads to a decrease of physical activity [1]. Nevertheless, in several studies, gradually increasing activity programs have proven to be important in the treatment of CFS [2–7]. Although CFS patients seem to have the belief that activity is harmful, the effect of exercise on symptoms and activity in CFS patients is not known.

Until now, only a few studies examined exacerbation of symptoms and decrease of physical activity after exercise. Most of these studies mainly concern physiological responses to treadmill or cycle exercise tests in CFS. Two uncontrolled studies, one measuring on the seventh day after exercise [8] and one everyday up to 7 days [9], did not find any adverse effects of exercise on symptoms and activity. Conversely, two controlled studies did find an increase of fatigue after exercise. One study measured after 24 h [10], 1 up to 4 days [11].

In the studies mentioned, assessment took place by just asking for adverse after-effects following testing [8], by questionnaires like the modified version of the Profile Of Mood Scales (POMS; [9–11]), an activity restriction index [9], a symptom log [9], and daily ratings of fatigue [11]. Only in one study was an accelerometer used to measure the effect of exercise on physical activity. An unexplained reduction in activity on the fifth day after the exercise test was found for CFS but not for controls [12].

* Corresponding author. Tel.: +31 24 3613608; fax: +31 24 3613425.
E-mail address: e.bazelmans@mps.umcn.nl (E. Bazelmans).
[1] Tel.: +31 24 3613608.
[2] Tel.: +31 24 3612430.
[3] Tel.: +31 24 3614763.
[4] Tel.: +31 24 3233217.

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It has been shown that self-report questionnaires on physical activity do not correlate very well with accelerometer readings [13]. Whereas questionnaires that require simple ratings of actual activity were related to the accelerometer, instruments that require general subjective interpretations of activity were not. Furthermore, questionnaires like the POMS do not seem sensitive for day-to-day changes in repeated measurements. Standardized self-observation measures seem more appropriate to assess fluctuations in fatigue [14,15].

The purpose of the current study was to investigate the effect of a maximal exercise test (MET) on fatigue, muscle pain, rest, and activity on the days surrounding the exercise test. In a former study [16], the physiological aspects of a MET in CFS compared with controls were described. No significant differences in physical fitness between CFS patients and their controls were found. In this same study, self-observation measurements, as well as an accelerometer, were used. These results are presented now. Symptoms and activity were measured the hours before and after the test, as well as the days before, of, and after the exercise test. CFS patients were compared with neighborhood controls. It was expected that after the MET for CFS patients, as well as for controls fatigue, muscle pain and rest will be increased and physical activity will be decreased as compared with baseline. In this context, a significant difference in the extent as well as in the duration of changes in symptoms and activity between CFS and controls was anticipated. CFS patients were expected to experience a more severe increase of symptoms, of longer duration, and a more prevalent and longer lasting decrease of activity.

Methods

Participants

Patients were recruited from a group of CFS patients diagnosed at the General Internal Medicine outpatient clinic of the University Medical Center Nijmegen, a national referral expert center for CFS. The diagnosis CFS was made after a thorough medical investigation. All patients fulfilled the Fukuda criteria for CFS [17].

As a rule, screening questionnaires were sent to all patients diagnosed with CFS at the outpatient clinic. For the present study, only CFS patients with a Checklist Individual Strength (CIS) fatigue severity score of 40 or more and a total score of the Sickness Impact Profile (SIP)-8 of more than 800 were included to guarantee severe fatigue and disability ([18]; see instruments). With these operational criteria, severe fatigue and impairment in CFS can be distinguished from fatigue and impairment in other conditions [18]. Finally, patients had to be able to recruit a neighbor of the same gender and about the same age, as a control. Twenty-six CFS patients, living in the surroundings of our hospital, were asked to participate. Twenty of these met our additional CIS and SIP-8 criteria and found a neighborhood control. Prior to their commitment, all participants were completely informed about the method and procedure of the study. The physiological characteristics of these participants have been described in detail elsewhere [16].

Measures

Checklist Individual Strength

The subscale fatigue severity of the fatigue questionnaire CIS [18] was used to assess overall fatigue. The subscale fatigue consists of eight items asking for fatigue severity during the last 2 weeks. Each item was scored on a seven-point Likert scale, thus, the range is 8-56. Cronbach's alpha is .88. This subscale has proved its usefulness in several studies and, for instance, distinguishes fatigue in CFS patients from fatigue in patients with functional bowel disorder and healthy controls [18].

Sickness Impact Profile

Functional impairment was assessed using the SIP [19,20]. This questionnaire measures the influence of complaints in different areas of daily functioning. The following eight subscales were used: alertness behavior, sleep, homemaking, leisure activities, work, mobility, social interactions, and ambulation. The sum of the weights of items of these subscales is referred to as the SIP-8. These subscales of the SIP are often used in CFS and distinguish functional impairment in CFS patients from patients with several other physical complaints [18].

Maximal exercise test

A bicycle ergometertest with incremental load was used as an exercise test [21]. The workload was increased every minute in steps of 10% of estimated maximal workload to complete all MET in approximately 10 min. Steps varied from 10 to 30 W/min. Participants were verbally encouraged to perform maximally until exhaustion. The time spent on the bicycle ergometer was 8.0 ± 2.3 min for CFS and 9.2 ± 1.9 min for the controls. The percentage of the predicted maximal workload reached, (value reached/predicted value)$\times$100, was 83% for controls and 70% for CFS.

Self-observation

A self-observation list was used to assess fatigue, muscle pain, and activity from 3 days before up to 5 days after the MET.

Daily assessment

Except for the day before, the day of, and the day after the MET, self-observation scores were obtained at breakfast, lunch, dinner, and bed time, with 9 a.m., noon, and 6 and 10 p.m. as a directive, on a scale from 0 to 4. For daily observed fatigue and daily observed muscle pain, 0 meant *no symptoms* and 4 meant *very severe symptoms*. For daily observed activity, 0 meant *not active at all* and 4 was *very active*. Scores were added up for each day and divided by four, resulting in a score from 0 to 4 for daily observed fatigue, daily observed muscle pain, and daily observed activity. In addition, everyday, the time spent resting was asked for. Daily observed rest was defined as the number of minutes rest during a day. The scores for the daily data the day before, the day of, and the day after the MET were obtained as averages of the hourly scores. For daily observed fatigue, muscle pain, and activity, only the data obtained after performing the MET were used to compute the mean of the day the MET was performed.

Hourly assessment

On the day before, the day after, and the day of the MET, assessments of fatigue, muscle pain, and activity were made every hour to obtain hourly scores on the same scale as used in the daily assessment. On these 3 days, the time spent resting was asked for every hour and recorded as the number of minutes spent resting during the last hour.

Actometer

Physical activity was also assessed using the actometer, an accelerometer worn around the ankle for 2 weeks. The actometer consists of a piezoelectric sensor that is sensitive in three directions. Accelerations of the sensor larger than a predefined threshold are considered as activity and are stored into an internal memory. Each second the microcontroller reads and resets the counter of the actometer. The integration counter is set at 5 min, providing every 5 min an activity score that is stored into the internal memory of the actometer. At the end of the registration period, data are fed into an external computer. The actometer has been used in several previous studies on CFS and is a good measure of actual physical activity (see, for instance, Refs. [13,22]).

Daily assessment

Based on the mean of the recorded number of movements every 5 min during a day, for each day, an average daily actometer score was computed. As for the self-observation data, on the day of the MET, only the data obtained after the MET took place were used to compute the mean of that day.

Hourly assessment

For the day before, the day of, and the day after the MET, mean scores per hour were computed as the mean of the recorded number of movements of every 5 min during the past hour.

Procedure

Daily procedure

All patients and controls were given the self-observation list and the actometer to keep for 3 days before up to 5 days after the MET. Daily scores of the 3 days before the MET were used to compute a baseline score. Daily scores obtained at the day of the MET and at the 5 days after the MET were compared with that of the baseline to detect the impact of the MET on symptoms and activity on a daily level (see statistical analyses).

Hourly procedure

Within each couple, a CFS patient and the control performed the MET at the same day of the week, and within all but three of the couples, the MET was also performed at the same time of the day, with a time difference of less than 1 h. Within three couples, the time difference of performing the MET was, respectively 1, 2, and 3 h. Because between couples, the time the MET was performed ranged from 9 a.m. to 4 p.m., complete hourly data are only available from 1 h before up to 6 h after the MET. Hourly data were collected the day of, the day before, and the day after the MET. To detect the impact of the MET on self-observed and actometer scores at an hourly level, hourly data obtained at the day of the MET were compared with the hourly data for the same relative time points on the day before and the day after the MET (see statistical analyses).

Statistical analyses

Data analyses were performed using SPSS (Version 8.0).

Analyses of baseline data

To control for day-to-day fluctuations, baseline scores were computed as the average score of the 3 days before the MET. To test whether these baseline scores were stable, they were analyzed by 2 (Group)×3 (Day) general linear model repeated-measures analyses of variance (GLM RMANOVA).

Analyses of daily data

To analyze the impact of the MET on self-observed and actometer scores over days, a 2 (Group)×7 (Day) GLM RMANOVA was used, in which the day of and the days after the MET were compared with baseline. Simple contrasts with baseline data were tested for each group separately.

Analyses of hourly data

As within-day fluctuations in self-observed and actometer scores were to be expected [23,24], diurnal patterns of the day before, the day of, and the day after the MET were

Table 1
Characteristics of CFS patients and controls (% or mean (SD); median (25th and 75th percentile) for SIP-8)

	CFS (n=20)	Control (n=20)
(%) female	60	60
Age (years)	34.1 (8.3)	32.8 (7.2)
Fatigue (CIS; range 8–56)	51.7 (5.1)	13.4 (5.1)
Functional impairment (SIP-8)	1743 (1249–2058)	0 (0–0)
Duration of complaints (yrs)	3.2 (2.5)	–

compared using 2 (Group)×3 (Day)×7 (Hour) GLM RMANOVA. Additionally, as a secondary analysis, a 2 (Group)×3 (Day) GLM RMANOVA was performed for each hour separately. Within-groups simple contrasts of 1 day before the MET compared with, respectively, the day of the MET and 1 day after the MET were tested for each hour separately.

Because we were interested in whether changes in self-observed and actometer scores after exercise would differ between CFS patients and their controls, only interaction effects with group are reported. For the same reason, simple contrasts with baseline data were tested for each group separately. For exploratory reasons, the statistically significant results of these tests of contrasts are shown whether a statistically significant interaction effect could be obtained.

For all analyses, the significance level was set at .05. Effect sizes (η^2) are shown. Due to failing actometers, sample sizes concerning actometer data are 16 for CFS and

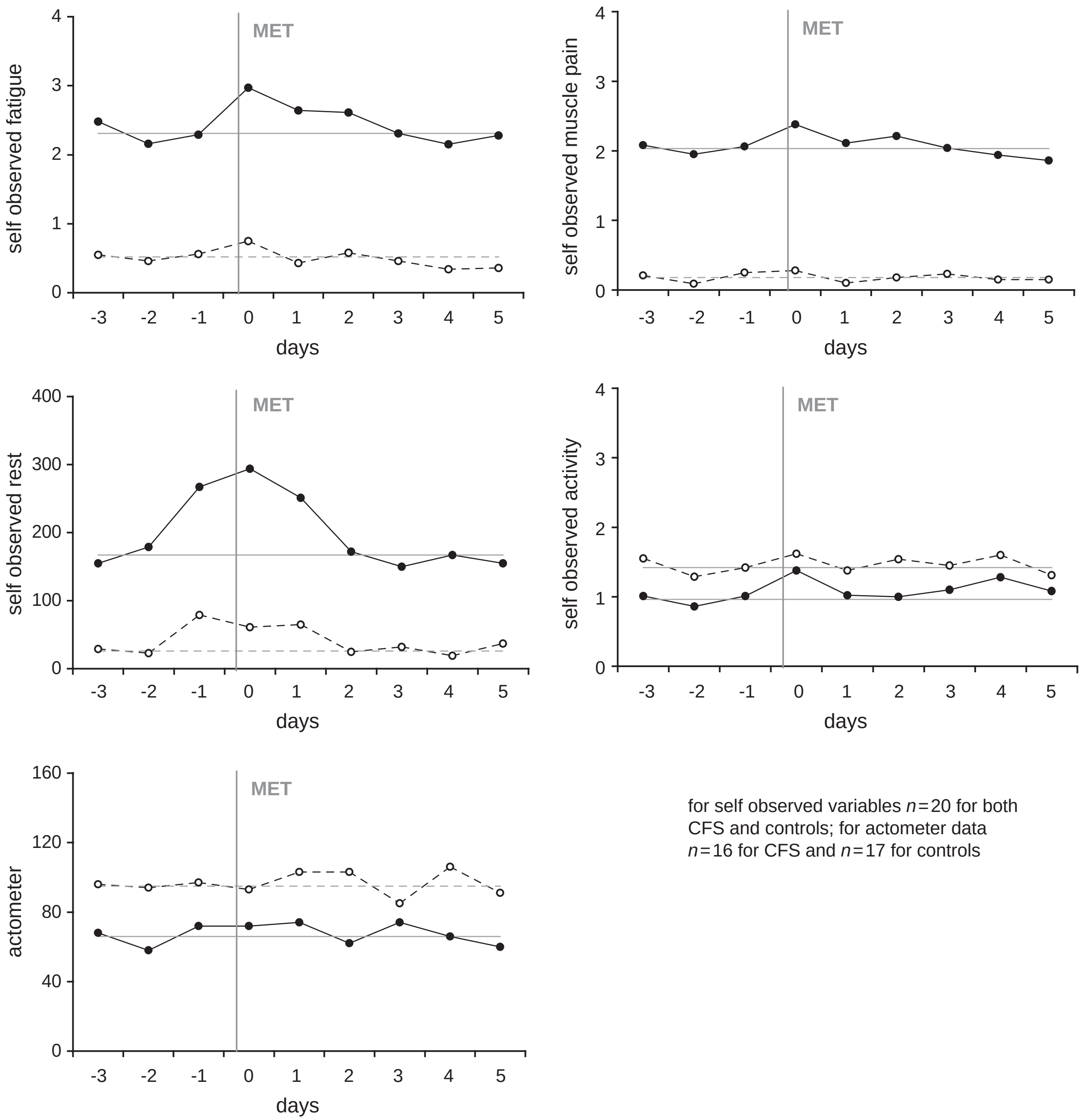

Fig. 1. Mean daily self-observed and actometer scores from 3 days before (−3) up to 5 days after (5) the MET for CFS (—; ●) and controls (- - -; ○); baseline is represented as a horizontal line (average of the 3 days before the MET; for daily observed rest, the average of the third and second days before the MET; CFS, —; controls, - - -).

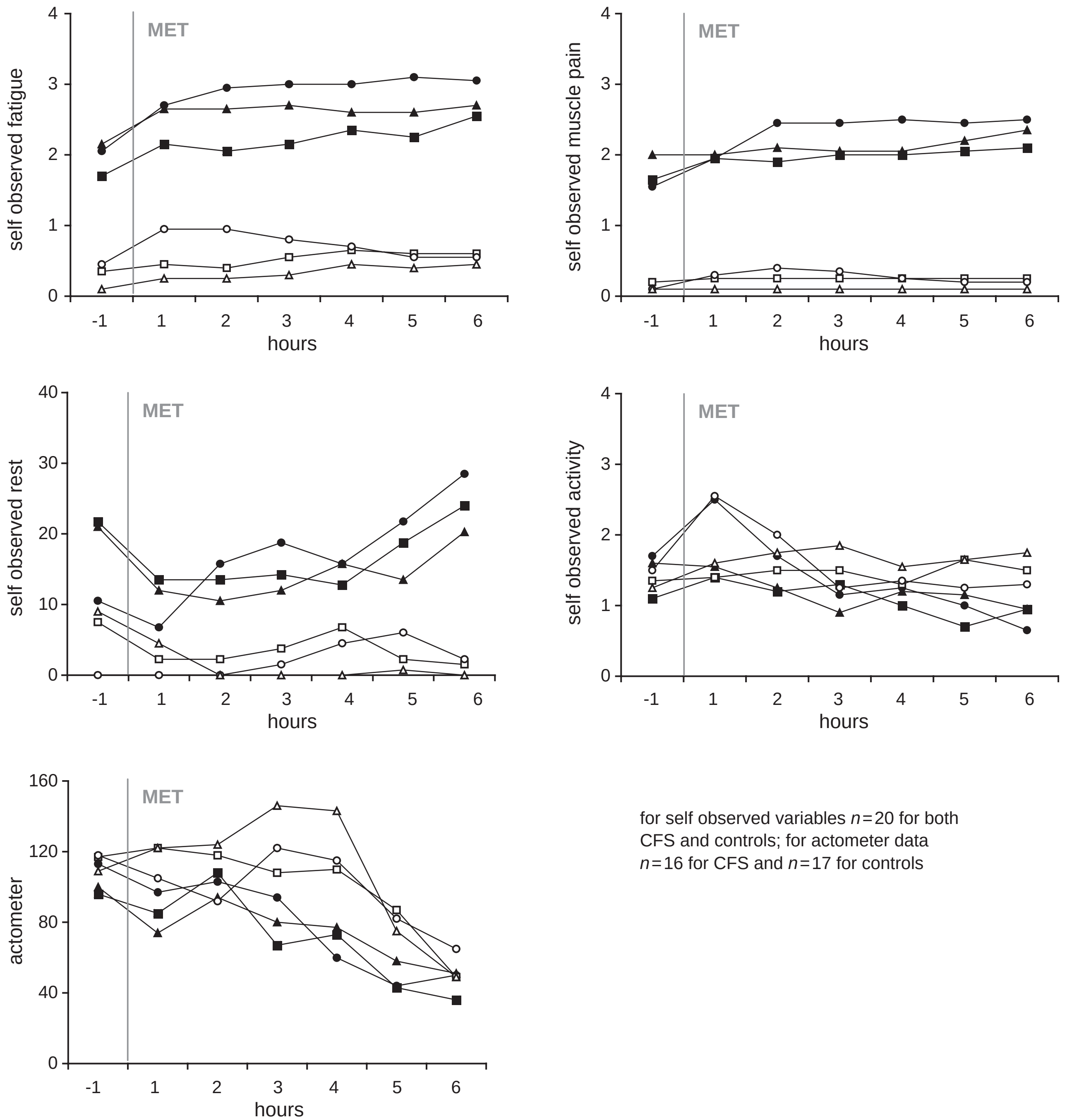

Fig. 2. Mean hourly self-observed and actometer scores for CFS (—; closed symbols) and controls (- - -; open symbols) 1 h before (−1) up to 6 h after (6) the MET, the day of the MET (●, ○), compared with the hourly data of the related points of time of the day before (■, □) and the day after (▲, △) the MET.

17 for controls. For all other variables, there are 20 participants in each group.

Results

Patient and control characteristics

Demographic data, CIS-fatigue, and SIP scores are shown in Table 1. Differences in CIS-fatigue, SIP-8, and duration of complaints were as expected.

Impact of the MET on fatigue, muscle pain, rest, and activity

Fig. 1 shows the means of all daily observed variables and the actometer from 3 days before up to 5 days after the MET for CFS and controls.

Baseline of the daily scores

For daily observed fatigue, daily observed muscle pain, daily observed activity, and the actometer, the baseline scores of the 3 days before the MET did not reveal any systematic interaction or within-subjects differences. For these variables, the means of these 3 days were used as a baseline. Analyses of the daily observed rest scores of the 3 days before the MET did show a significant within-subjects difference [F(2,37)=1.31, η^2=.38, P=.000]. No statistically significant group-by-day interaction effect was found. For daily observed rest, scores of 1 day before the MET seemed to deviate from the scores at the other two time points in both groups. No average differences were found between the means of daily observed rest 3 and 2 days before the MET. Therefore, for both groups, the mean of these days were used as a baseline for daily observed rest.

The daily scores of the days after the MET compared with baseline

For daily observed fatigue, a statistically significant day-by-group effect was found [F(6,33)=3.74, η^2=.38, P=.011]. The contrast procedure revealed that, for CFS, the day of, 1 day after, and 2 days after the MET, daily observed fatigue was significantly increased compared with baseline [F(1,38)=27.99, η^2=.42, P=.000; F(1,38)=10.98, η^2=.22, P=.002; and F(1,38)=6.88, η^2 =.15, P=.012, respectively]. For controls, none of the simple contrasts with baseline were statistically significant. A significant time-by-group effect was also found for daily observed rest [F(6,33)=2.66, η^2=.33, P=.033]. For CFS, the contrast procedure showed a

Table 2
Simple contrasts of hourly self observed and actometer scores comparing the day of and the day after the MET with the day before (the hours are relative to the time of the day the MET was taken), separately for CFS and controls

		Contrast between the day of and the day before the MET[a]						Contrast between the day after and the day before the MET[a]					
		CFS			Controls			CFS			Controls		
		F	η^2	P	F	η^2	P	F	η^2	P	F	η^2	P
Self observed fatigue													
Hour	−1			NS			NS	6.23	.14	.017			NS
	1	5.48	.13	.025	4.53	.11	.040	8.56	.18	.006			NS
	2	13.17	.26	.001	4.92	.11	.033	11.72	.24	.001			NS
	3	14.34	.27	.001			NS	11.11	.23	.002			NS
	4	11.68	.24	.002			NS			NS			NS
	5	18.61	.33	.000			NS			NS			NS
	6	8.66	.19	.006			NS			NS			NS
Self observed muscle pain													
Hour	−1			NS			NS			NS			NS
	1			NS			NS			NS			NS
	2			NS			NS			NS			NS
	3			NS			NS			NS			NS
	4	6.13	.14	.018			NS			NS			NS
	5	6.16	.14	.018			NS			NS			NS
	6	8.84	.19	.005			NS			NS			NS
Self observed rest													
Hour	−1	4.51	.11	.040			NS			NS			NS
	1	6.04	.14	.019			NS			NS			NS
	2			NS			NS			NS			NS
	3			NS			NS			NS			NS
	4			NS			NS			NS			NS
	5			NS			NS			NS			NS
	6			NS			NS			NS			NS
Self observed activity													
Hour	−1	5.78	.13	.021			NS	4.66	.11	.037			NS
	1	8.33	.18	.006	9.11	.19	.005			NS			NS
	2			NS			NS			NS			NS
	3			NS			NS			NS			NS
	4			NS			NS			NS			NS
	5			NS			NS	4.97	.12	.032			NS
	6			NS			NS			NS			NS
Actometer													
Hour	−1			NS			NS			NS			NS
	1			NS			NS			NS			NS
	2			NS			NS			NS			NS
	3			NS			NS			NS			NS
	4			NS			NS			NS	4.19	.12	.049
	5			NS			NS			NS			NS
	6			NS			NS	6.75	.18	.014			NS

[a] df [1,38]; for actometer df [1,31].

significant increase for daily observed rest between baseline and the day of the MET [$F(1,38)=39.65$, $\eta^2=.51$, $P=.000$], as well as between baseline and 1 day after the MET [$F(1,38)=22.62$, $\eta^2=.40$, $P=.000$]. In the control group, daily observed rest differed only significantly between 1 day after the MET and baseline [$F(1,38)=5.68$, $\eta^2=.13$, $P=.022$]. On daily observed muscle pain, daily observed activity, and the actometer, the average profiles of scores after the MET appeared not significantly different for the two groups.

Differences in hourly fatigue, muscle pain, rest, and activity scores the day before, the day of, and the day after the MET

The mean hourly self-observed scores of fatigue, muscle pain, rest, and activity, the day before, the day of, and the day after the MET are illustrated in Fig. 2. No statistically significant group-by-day-by-hour effects were found, neither for any of the hourly self-observed nor for the hourly actometer scores. Group-by-day GLM RMANOVAs on the hourly scores for each hour separately showed a day-by-group interaction effect for fatigue on the hour before [$F(2,37)=4.80$, $\eta^2=.21$, $P=.014$] and 1 [$F(2,37)=4.39$, $\eta^2=.19$, $P=.020$], 2 [$F(2,37)=4.54$, $\eta^2=.20$, $P=.017$], 3 [$F(2,37)=5.74$, $\eta^2=.24$, $P=.007$], and 5 h after the MET [$F(2,37)=5.74$, $\eta^2=.22$, $P=.010$]. Besides, a day-by-group interaction effect was found for self-observed activity 3 h after the MET [$F(2,37)=3.14$, $\eta^2=.16$, $P=.044$].

The accompanying contrast procedures are shown in Table 2.

Discussion

In CFS, fatigue after exercise increased more and was of longer duration as compared with healthy controls. Whereas for controls, fatigue returned to baseline after 2 h, for CFS, a significant increase of daily observed fatigue was found up to 2 days after the exercise test. Muscle pain was increased only in CFS and only on the day of the exercise test, specifically 4 to 6 h after the MET. This increase in CFS, however, is not significantly different from the increase of muscle pain in controls.

A striking result is that, for CFS as well as for controls, minutes spent resting increased the day before the exercise test. Both groups seem to anticipate the exercise test. Although both groups also reported more time spent resting the day after the MET, the reported minutes rest on the day of the exercise test increased more for CFS than for controls. For both groups, the daily observed minutes spent resting returned to normal not earlier than on the second day after the exercise test. Due to an increase of daily observed rest on the day before, the day of, and the day after the MET for both groups, diurnal patterns did not show many differences. CFS patients only seemed to spend fewer minutes resting during the hour before as well as the hour after the MET, compared with the related hourly scores of the day before. Probably, this is a consequence of traveling to the hospital for the exercise test.

Contrary to what was expected, the actometer did not reveal a decrease of physical activity after the exercise test. The self-observed daily level of activity increased in CFS the day of the MET, when compared with baseline. Furthermore, both CFS patients and controls considered themselves to have been more active during the hour after the exercise test, whereas CFS patients also showed a somewhat increased daily observed level of activity the hour before the exercise. Probably, again, these reported increases of activity surrounding the exercise test are a consequence of the participant's travel to the hospital. The few other statistically significant findings concerning activity are hard to explain. Whereas these late effects were not hypothesized and are not congruent, they probably have to be considered random fluctuations. Thus, although there are some findings that activity increases after exercise, no decrease of activity after exercise was found.

One might argue that the MET was not strenuous enough to find an effect on activity. This is, however, unlikely. Data concerning physiological aspects of the MET showed that both CFS patients and controls reached a highly increased level of perceived exertion at maximal workload [16]. As we have shown now, CFS patients were even more fatigued several days thereafter, while their level of physical activity remains unchanged.

Confidence intervals for the actometer were broad for both groups (data not shown). Therefore, changes are not easily significant, and interpreting the actometer scores is difficult. Possibly, the heterogeneity of the CFS group might hide effects for subgroups of patients. It has been found that, based on their level of physical activity as assessed with the actometer, different groups of CFS patients can be distinguished [22]. Some CFS patients appeared to be really inactive, called passive CFS patients, whereas others are still rather active, called pervasively active CFS patients. In between, most CFS patients have a fluctuating activity pattern, called moderately active. One might hypothesize that the impact on symptoms and activity of an exercise test might be more present in passive CFS patients. In the present study, sample sizes are too small to test this hypothesis. Only three CFS patients in our study were passive patients. This percentage of passive CFS patients in our sample is congruent with the number of passive CFS patients in other samples [22].

Although actometer results seem rather congruent with daily observed activity scores, there is a striking discrepancy between the actometer results and self-observed minutes spent resting. Post hoc analyses do not show any significant correlations between the actometer and daily observed rest or daily observed activity. This agrees with findings of Vercoulen et al. [13], who found that daily observed activity is a subjective rating of activity, whereas the actometer is a behavioral measure. The same might account for daily observed rest. It might be that CFS patients, as well as controls, perceive themselves to rest more, but actually do not. An alternative explanation is that participants do not so much diminish physical activities but withdraw from other, e.g., mental and social activities.

Hence, the perception of CFS patients that they remain more fatigued for days after strenuous exercise is in accordance with the findings in this study. However, their level of physical activity does not change. Still, both CFS patients and controls report more minutes spent resting the day before, the day of, and the day after exercise.

References

[1] Silver A, Haeny M, Vijayadurai P, Wilks D, Pattrick M, Main CJ. The role of fear of physical movement and activity in chronic fatigue syndrome. J Psychosom Res 2002;52:485–93.

[2] Sharpe M, Hawton K, Simkin S, Suraway C, Hackman A, Klimes I, Peto T, Warell D, Seagroatt V. Cognitive behaviour therapy for the chronic fatigue syndrome: a randomised controlled trial. BMJ 1996; 312:22–6.

[3] Deale A, Chalder T, Marks I, Wessely S. Cognitive behavior therapy for chronic fatigue syndrome: a randomized controlled trial. Am J Psychiatry 1997;154:408–14.

[4] Fulcher KY, White PD. Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome. BMJ 1997; 314:1647–52.

[5] Wearden AJ, Morriss RK, Mullis R, et al. Randomised, double-blind, placebo-controlled treatment trial of fluoxetine and graded exercise for chronic fatigue syndrome. Br J Psychiatry 1998;172:485–90.

[6] Powell P, Bentall RP, Nye FJ, Edwards KHT. Randomised controlled trial of patient education to encourage graded exercise in chronic fatigue syndrome. BMJ 2001;322:387–90.

[7] Prins JB, Bleijenberg G, Bazelmans E, Elving LD, de Boo TM, Severens JL, van der Wilt GJ, Spinhoven P, van der Meer JWM. Cognitive behaviour therapy for chronic fatigue syndrome: a multicenter randomised controlled trial. Lancet 2001;357:841–7.

[8] Mullis R, Campbell IT, Wearden AJ, Morriss RK, Pearson DJ. Prediction of peak oxygen uptake in chronic fatigue syndrome. Br J Sports Med 1999;33:352–6.

[9] Clapp LL, Richardson MT, Smith JF, Wang M, Clapp AJ, Pieroni RE. Acute effects of thirty minutes of light-intensity, intermittent exercise on patients with chronic fatigue syndrome. Phys Ther 1999; 79:749–56.

[10] LaManca JJ, Sisto SA, Zhou XD, Ottenweller JE, Cook S, Peckerman A, Zhang Q, Denny TN, Gause WC, Natelson BH. Immunological response in chronic fatigue syndrome following a graded exercise test to exhaustion. J Clin Immunol 1999;19:135–42.

[11] Sisto SA, LaManca J, Cordero DL, Bergen MT, Ellis SP, Drastal S, Boda WL, Tapp WN, Natelson BH. Metabolic and cardiovascular effects of a progressive exercise test in patients with chronic fatigue syndrome. Am J Med 1996;100:634–40.

[12] Sisto SA, Tapp WN, LaManca JJ, Ling W, Korn LR, Nelson AJ, Natelson BH. Physical activity before and after exercise in women with chronic fatigue syndrome. QJM 1998;91:465–73.

[13] Vercoulen JHMM, Bazelmans E, Swanink CMA, Fennis JFM, Galama JMD, Jongen PJH, Hommes O, van der Meer JWM, Bleijenberg G. Physical activity in chronic fatigue syndrome: assessment and its role in fatigue. J Psychiatr Res 1997;31:661–73.

[14] Dougall AL, Baum A, Jenkins FJ. Daily fluctuation in chronic fatigue syndrome severity and symptoms. J Appl Biobehav Res 1998;3:12–28.

[15] Jason LA, King CP, Frankenberry EL, Jordan KM. Chronic fatigue syndrome: assessing symptoms and activity level. J Clin Psychol 1999;55:411–24.

[16] Bazelmans E, Bleijenberg G, van der Meer JWM, Folgering H. Is physical deconditioning a perpetuating factor in chronic fatigue syndrome? A controlled study on maximal exercise performance and relations with fatigue, impairment and physical activity. Psychol Med 2001;31:107–14.

[17] Fukuda K, Strauss SE, Hicki I, Sharpe MC, Dobbins JG, Komaroff A, The International Chronic Fatigue Study Group. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med 1994;121:953–9.

[18] Vercoulen JHMM, Swanink CMA, Fennis JFM, Galama JMD, van der Meer JWM, Bleijenberg G. Dimensional assessment of chronic fatigue syndrome. J Psychosom Res 1994;38:383–92.

[19] Bergner M, Bobbit RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. Med Care 1981;19:787–805.

[20] Jacobs HM, Luttik A, Touw-Otten FWMM, Melker RA. De "Sickness Impact Profile": resultaten van een valideringsonderzoek van de Nederlandse versie. Ned Tijdschr Geneeskd 1990;134: 1950–4.

[21] Folgering H, van Doorn P, Cox N. A prediction equation for Wmax in COPD-patients. Eur Respir J 1988;1(Suppl 1):67S.

[22] Van der Werf SP, Prins JB, Vercoulen JHMM, van der Meer JWM, Bleijenberg G. Identifying physical activity patterns in chronic fatigue syndrome using actigraphic assessment. J Psychosom Res 2000;49: 373–9.

[23] Wood C, Magnello ME, Sharpe MC. Fluctuations in perceived energy and mood among patients with chronic fatigue syndrome. J R Soc Med 1992;85:195–8.

[24] Stone AA, Broderick JE, Porter LS, Krupp L, Gnys M, Paty JA, Shiffmann P. Fatigue and mood in chronic fatigue syndrome patients: results of a momentary assessment protocol examining fatigue and mood levels and diurnal patterns. Ann Behav Med 1994; 16:228–34.