

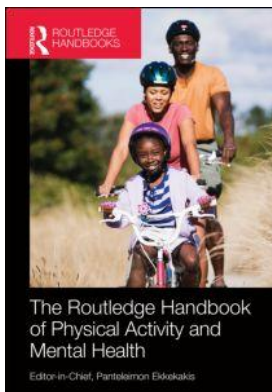
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Tired of Being Sedentary

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Jo Nijs, Mira Meeus, Jessica Van Oosterwijck, Kelly Ickmans, Inge van Eupen, Daphne Kos

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TIRED OF BEING SEDENTARY

Physical activity as a treatment goal in patients with chronic fatigue syndrome

Jo Nijs, Mira Meeus, Jessica Van Oosterwijck, Kelly Ickmans, Inge van Eupen, and Daphne Kos

Chronic fatigue syndrome (CFS) describes a disorder consisting of chronic debilitating fatigue that cannot be explained by any known chronic medical or psychological condition (Fukuda et al., 1994). While a variety of case definitions exist, often with varying nomenclatures (reviewed in Christley, Duffy, & Martin, 2011), the most widely accepted for research purposes remains the 1994 Centers for Disease Control and Prevention definition (Harvey, Wadsworth, Wessely, & Hotopf, 2008). The core feature of a CFS diagnosis is the exclusion of any active medical condition that may explain the presence of the symptoms (e.g., severe obesity, cancer hypothyroidism, primary sleep disorders, rheumatoid arthritis, multiple sclerosis, Hepatitis B or C, major depressive disorders with psychotic or melancholic features, bipolar affective disorders, schizophrenia, dementia, alcohol abuse; Fukuda et al., 1994). CFS is a disorder affecting approximately 0.5 percent of the population (Jason et al., 1999b).

A second requirement for CFS diagnosis entails the presence of a new onset, unexplained, and persistent fatigue, unrelated to exertion and not substantially relieved by rest. Importantly, the fatigue should be severely disabling, in a way that causes substantial reductions in physical activity levels. Finally, four or more of the following symptoms should be present for 6 months or longer: impaired memory or concentration; extreme, prolonged exhaustion and sickness as a result of physical or mental exertion (post-exertional malaise); unrefreshing sleep; muscle pain; pain in multiple joints; headaches of a new kind or greater severity; sore throat and tender lymph nodes (cervical or axillary).

Thus, CFS diagnostic criteria imply a substantial reduction in activity levels. In most cases, this implies a major decrease in physical activity level. Yet patients with CFS do not choose to be physically inactive. They are tired of being inactive. Without appropriate treatment, they are unable to increase their physical activity level without experiencing a relapse.

This chapter provides an overview of the current understanding of physical activity in patients with CFS. We discuss and summarize research data concerning CFS physical activity levels and patterns and explain that effective treatments are available to improve physical activity levels in patients with CFS. Finally, we address some methodological issues and directions for future research in this important area.

Physical activity level in patients with CFS

A large national birth cohort study revealed that continuing to be active despite increasing fatigue is likely a crucial step in the development of CFS (Harvey et al., 2008). Once CFS is established, the situation changes dramatically. Post-exertional malaise becomes a major characteristic of the illness. This implies that symptoms like fatigue and pain are typically made worse after modest amounts of exercise (Clapp et al., 1999), after increased daily physical activity (Black, O'Conner, & McCully, 2005), and after a submaximal exercise stress test (Bazelmans, Bleijenbergh, Voeten, van der Meer, & Folgering, 2005; Lapp, 1997). Post-exertional malaise in CFS is accompanied by a delayed recovery from exercise (Paul, Wood, Behan, & Maclaren, 1999). Hence, rest and activity avoidance could be a way to cope with CFS-related post-exertional malaise (Vercoulen et al. 1996). These observations indirectly imply that patients with CFS perform less physical activity. In fact, it suggests that patients with CFS are too tired to be physically active. Is there research data to support this view?

Nijs et al. (2011) in a recent systematic literature review concluded that all published studies on physical activity in CFS found reduced habitual physical activity among patients with CFS compared to healthy controls (Bazelmans, Bleijenbergh, van der Meer, & Folgering, 2001; Black, O'Conner, & McCully, 2005; Jason et al., 1999a; Sisto et al., 1998; Vercoulen et al., 1997). In total, 99 patients with CFS and 101 healthy control subjects were studied. Each of the studies used real-time continuous activity monitoring (accelerometers). Importantly, some studies used sedentary healthy participants for comparison. These findings provide research data to support the notion that patients with CFS, on average, are physically inactive and often perform less physical activity than sedentary control subjects (Nijs et al., 2011).

The question therefore arises, why are people with CFS physically inactive? Avoidance behavior toward physical activity is likely to influence physical activity level and exercise performance. CFS patients have been shown to perform less frequently specific activities expected to result in high fatigue levels and high fatigue expectations are related to low activity levels (Vercoulen et al., 1997). Kinesiophobia, a specific kind of fear-avoidance behavior, is defined as "an excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or reinjury" (Kori, Miller, & Todd, 1990). In patients with CFS, kinesiophobia represents a clinically important feature (i.e., related to disability), but does not appear to be a determinant of physiological exercise capacity (Nijs, De Meirleir, & Duquet, 2004; Nijs, Vanherberghen, Duquet, & De Meirleir, 2004; Silver et al., 2002). This observation is in line with a study showing stronger voluntary efforts (i.e., stronger brain signals recorded with electroencephalogram) during motor tasks in CFS patients compared to healthy controls (Siemionow, Fang, Calabrese, Sahgal, & Yue, 2004). This implies that during exercise capacity testing, patients with CFS do not avoid maximal exertion due to kinesiophobia; instead, their brain commands the muscles to exercise, but the body is incapable of performing.

On the other hand, overactivity or workaholism may be important predisposing and perpetuating factors for CFS. Patients with CFS are often perfectionists and frequently try very hard to meet their own and others' requirements (Van Houdenhove, Onghena, Neerinckx, & Hellin, 1995). Sustained physical or mental effort may, in susceptible individuals, eventually lead to neuro-endocrine and immunological dysfunctions (Van Houdenhove, Neerinckx, Onghena, Lysens, & Vertommen, 2001). This reasoning is in line with our current understanding of post-exertional malaise in people with CFS.

Several investigators have shown that overly vigorous exercise (De Becker, Roeykens, Reynders, McGregor, & De Meirleir, 2000; Lapp, 1997; Nijs, De Meirleir, Wolfs, & Duquet, 2004) or even merely a 30 percent increase in activity (Wong et al., 1992) frequently triggers a

relapse, which may explain at least part of the physical inactivity seen in CFS patients. This post-exertional malaise has been linked to acute immune changes following physical activity that exceeds a CFS patient's physical capabilities (Jammes, Steinberg, Mambrini, Brégeon, & Delliaux, 2005; Nijs et al., 2010; Sorensen et al., 2003). Fatigue and other CFS characteristics like post-exertional malaise make it difficult, if not impossible, to be physically active. Anyone who has worked with CFS patients can confirm they do not choose to be physically inactive. On the contrary, patients with CFS are tired of living a sedentary life. Current rehabilitation approaches for CFS emphasize the importance of pacing daily activities and respect for the physical and mental limitations inherent to CFS (Nijs, Paul, & Wallman, 2008). This approach aims at preventing post-exertional malaise in patients with CFS (Nijs et al., 2008) and will be explained in more detail below.

Physical activity patterns in CFS patients

In addition to the reduced activity level compared to the premorbid level or to healthy controls, people with CFS display an abnormal activity pattern: their lifestyle appears to be characterized by activity peaks and longer bouts of rest after activity (Van der Werf, Prins, Vercoulen, van der Meer, & Bleijenberg, 2000). This was confirmed by a recent literature review, which concluded patients with CFS have lower and shorter average activity peaks, followed by longer rest periods (van Weering, Vollenbroek-Hutten, Kotte, & Hermens, 2007). Resting and activity avoidance could be a way to cope with the illness (Vercoulen et al., 1996).

Based on their behavior, patients with CFS can be categorized in two subgroups. One group comprises those who feel helpless and avoid activity, resulting in extremely passive behavior. The second group displays a highly variable activity pattern. At "good" moments they try to move mountains, leading to exhaustion and longer periods of recovery. Both types of physical behavior patterns appear to be maladaptive (Moss-Morris, Sharon, Tobin, & Baldi, 2005).

Given the nature of CFS it seems rational to assume patients with CFS present a more fluctuating activity pattern, with greater variations and a pronounced staggering of activities during the day. Concerning the staggering of activities during the day, we found higher ratios (peak activity/average activity) in patients with CFS (Meeus et al., 2011). Patients with CFS tended to concentrate their activities more in peaks (probably at their better moments), instead of dispersing them, although the difference in ratios (peak activity/average activity) between CFS and healthy controls was not statistically significant. Additionally, fluctuations in activity patterns during the complete assessment period were not significantly different between patients and controls. In summary, we found no evidence for important variations in the activity pattern of patients with CFS during the day, or day by day (Meeus et al., 2011).

In the same study (Meeus et al., 2011), we also asked the question: Is the physical activity pattern of patients with CFS related to symptom variations? Sedentary activities and staggering of physical activity were negatively correlated to symptom severity and variation on the same day and the following day (Meeus et al., 2011). This implies patients who concentrated their physical activity more in peaks did so on days they experienced fewer symptoms. Light, moderate, and vigorous activity, as well as average activity and the activity peak, were positively correlated with symptom severity and variation on the same day and the subsequent day, indicating patients experienced more symptoms when they were more active. In summary, the more patients with CFS are sedentary and the better activity is dispersed throughout the day, the fewer symptoms and variations they experience on the same and the following day (Meeus et al., 2011).

Finally, it is important to study biological factors in relation to physical activity in patients with CFS. Few studies have addressed this issue. We recently reported that activity-related

symptom fluctuations in patients with CFS are not likely due to nitric oxide (NO) increases in response to normal physical activities (Meeus et al., 2010). NO was examined because it is known to increase the excitability of the central nervous system and regulate vascular tone in the tissues, including working muscles during exercise. When comparing CFS patients with healthy sedentary controls, no significant differences in serum NO amounts were observed. Variation in NO levels over the 1-week observation period was unrelated to daily activity levels in either group (Meeus et al., 2010). These findings corroborate our previous work, showing that neither post-exertional malaise nor impaired endogenous pain inhibition following exercise in patients with CFS is due to circulating NO levels (Meeus et al., 2010).

How to improve physical activity level and pattern during treatment

From what has been explained above, it seems plausible to include activity management in the comprehensive treatment of patients with CFS. Activity management is generally included in cognitive behavioral programs for CFS, and there is good evidence in support of the effectiveness of cognitive behavioral therapy for patients with CFS (Knoop, Bleijenberg, Gielissen, van der Meer, & White, 2007; Price, Mitchell, Tidy, & Hunot, 2008; Prins et al., 2001). Three weeks of pacing self-management is accompanied by a modest improvement in symptom severity and daily functioning (Nijs et al., 2009). The outcome of the latter study calls for a randomized controlled clinical trial to examine the effectiveness of pacing self-management for patients with CFS. Our group has completed such a trial and the results are in progress.

Self-management for people with CFS involves encouraging them to pace their activities and respect their physical and mental limitations (Pardaens, Haagdorens, Van Wambeke, Van den Broeck, & Van Houdenhove, 2006; Shephard, 2001). This strategy has been termed “pacing” and involves encouraging the patient to achieve an appropriate balance between activity and rest to avoid exacerbating symptoms. It requires the patient to set realistic activity goals on a daily basis (CFS/ME Working Group, 2001; Shephard, 2001) and to regularly monitor and manipulate activity in terms of intensity, duration, and rest periods to avoid possible over-exertion, which can result in worsening symptoms (CFS/ME Working Group, 2001; Shephard, 2001). Pacing takes into account the considerable fluctuations in symptom severity (Shephard, 2001) and delayed recovery from exercise that typically occurs in patients with CFS (Paul et al., 1999). This approach should not be confused with “adaptive pacing” (White et al., 2007), a strategy that advocates adapting to CFS. Such a strategy is based on the premise that people with CFS have a very low chance of recovery. In contrast, pacing activity self-management is an important aspect of the first phase of a comprehensive rehabilitation program for CFS, comprising a stabilization and subsequent grading phase (Nijs et al., 2008; Nijs, Van Oosterwijck, & Meeus, 2009). Graded activity and graded exercise therapy are typically used in the grading phase, and aim at increasing daily physical activity levels (e.g., Nijs et al., 2008). Graded activity implies the gradual increase of daily physical activity level, as well as the gradual increase in cognitive and social activities (Figure 30.1).

How should clinicians (physical therapists, occupational therapists, psychologists, etc.) provide activity self-management to their patients with CFS? The physical limits of the body should be respected in order to break out of the vicious circle of symptom exacerbations, avoidance, passivity, and further deconditioning. The pacing principle offers such a solution: limited periods (limits in proportion to the actual capabilities) of low-intensity activity, alternated with rest periods of the same duration.

Depending on the individual characteristics of the patient, activity self-management can be offered in a symptom- and time-contingent approach. Given mounting evidence supporting the

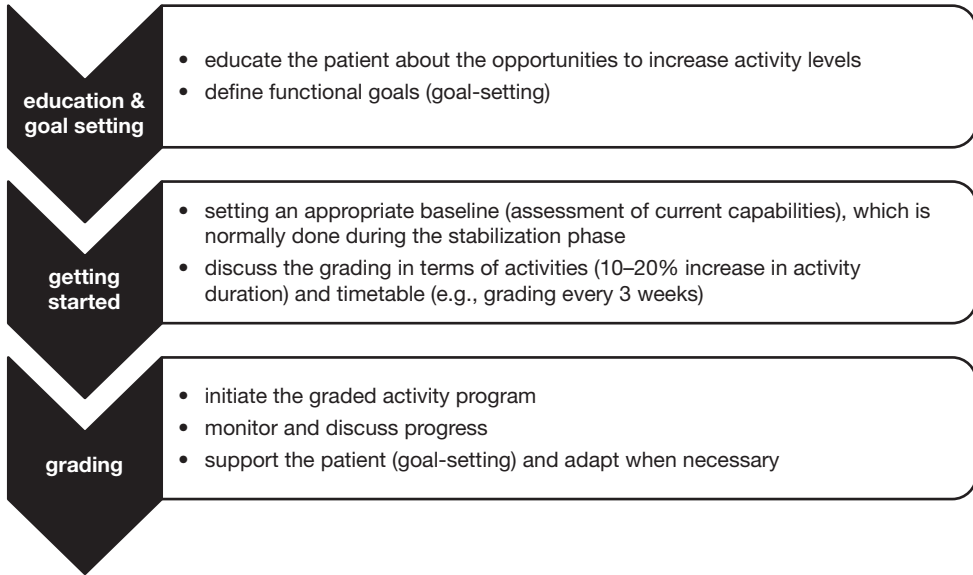


Figure 30.1 Grading phase: content of graded activity.

presence of central nervous system sensitization in CFS (Meeus, Nijs, Huybrechts, & Truijen, 2010; Meeus, Roussel, Truijen, & Nijs, 2010; Meeus, Nijs, Van de Wauwer, Toeback, & Truijen, 2008; Van Oosterwijck et al., 2010), small symptom variations should not be interpreted as signs of (new) tissue damage, but rather as “noise” produced by the hypersensitive central nervous system. Hence, a time-contingent approach seems rational even during the stabilization phase, and can prepare the patient for the graded activity approach during the grading phase. However, care must be taken not to over-exert the patient, because that may further increase the hypersensitivity of the central nervous system. The duration of daily activities should be adapted to the patient’s capabilities, accounting for the physical and cognitive limitations inherent to the illness. Therefore, the duration of the activities should be carefully supervised by the clinician providing activity self-management. Pacing self-management techniques encourage a behavioral change and at the same time acknowledge the physical aspects of the illness.

Methodological issues in relation to physical activity research in CFS

The good thing about physical activity research in CFS is the fact that all findings point in the same direction (i.e., reduced physical activity in CFS). This is important for an illness with a long history of disagreement between scientists and conflicting data across studies. However, methodological issues should not be ignored. Physical activity monitoring in CFS research has been conducted with accelerometers worn at the wrist or the leg. Both of these anatomical locations might generate somewhat biased findings. However, accelerometers worn at the wrist are preferred. For example, many CFS patients experience ironing as a fatiguing task, but leg-worn activity monitors do not assess the motion associated with this activity.

Another issue is the fact that cognitive tasks are often experienced as fatiguing for patients with CFS. Physical activity monitors do not register such activities. Still, the fact that accelerometers now have omnidirectional sensors implies they permit valid real-time physical activity monitoring of movements in all directions. This represents an important methodological

strength of physical activity research. Finally, patient employment status is an important concern because differences in activity level often appear between weekdays and weekend days. Further study in this area should consider possible bias due to work schedules and professional activities.

Future directions

Further work in this area should examine possible additional effects of physical activity interventions in patients with CFS. For example, to date, no data have been published on the extent that activity management contributes to the effectiveness of cognitive behavioral therapy in CFS patients. Cognitive behavioral therapy may be equally effective without inclusion of activity management. However, cognitive behavioral therapy might (in part) rely on activity management for its effectiveness. These are important questions, especially when we want to improve interventions targeting physical activity in patients with CFS.

Another future direction entails the study of the autonomic response of patients with CFS to daily physical activities like stair climbing or using a vacuum cleaner. Altered autonomic nervous system reactivity has been shown repeatedly in CFS patients (De Becker et al., 1998; Newton et al., 2009; Newton, Davidson, et al., 2007; Newton, Okonkwo, et al., 2007), but these studies used laboratory tests rather than real-life situations. It remains to be examined whether the stress response system of patients with CFS properly handles everyday physical stressors like stair climbing. This is important for rehabilitation purposes, as rehabilitation specialists should aim at increasing the physical capacity of CFS patients to cope with everyday stressors.

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