EXERCISE STATUS IN CHRONIC FATIGUE SYNDROME

by

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B.Sc. (Hons.) (University of Adelaide, 1997)

A thesis submitted for the degree of

DOCTOR OF PHILOSOPHY

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April 2006

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ABSTRACT

Chronic fatigue syndrome (CFS) is a condition characterised by profound physical and mental fatigue that is markedly exacerbated by physical exertion. Despite numerous hypotheses, its aetiology remains unknown and there is no agreed pathology or diagnostic laboratory test. No curative treatment has been found and current therapeutic strategies are directed toward symptom relief and functional improvement. Of these, graded exercise therapy (GET) is widely recommended as the best option for improving functional status by correcting the progressive loss of physical fitness that has been associated with the illness. The excessive fatigue experienced by CFS patients, both during and following exercise, has meant that this management option has been met with much caution. Such a reaction may not be entirely unjustified given that the evidence for a reduced physical fitness is by no means absolute. This issue was first highlighted during a series of pilot studies in our laboratory, examining potassium release during exercise in patients with CFS, where normal values for physical fitness, i.e. maximal oxygen uptake, were obtained using a sub-maximal predictive test. While predictive tests are notoriously unreliable, this finding raised the concern that if physical fitness is not reduced, then the current recommendation of GET may be based on a false premise. Furthermore, not only did a review of the methods of exercise testing and data analysis employed in many previous

studies expose serious flaws, but the efficacy of GET must also be questioned given the lack of evidence in published studies that it had any affect on the physiological aspects of their exercise status.

The reasons outlined above led to the focus of these doctoral studies on the exercise status of patients with CFS. This was examined in 33 patients with CFS, diagnosed by the same physician according to current international criteria, and compared with that of healthy, sedentary control subjects matched for age and sex.

In the first study, described in Chapter 3, maximal oxygen uptake ($\dot{V}O_{2max}$), the classic benchmark of exercise status, was measured in CFS patients and compared with that of control subjects. The exercise protocol employed to define $\dot{V}O_{2max}$ was of long-established design and used well-accepted criteria to identify a maximal effort. In this cohort of patients, $\dot{V}O_{2max}$ was not reduced, being not different from either age-predicted values or from that of control subjects. In addition, no other aspect of their cardio-respiratory responses to incremental exercise was different from control subjects, in particular, resting heart rate, heart rate reserve and maximal heart rate were not different, nor was the manner in which heart rate increased during exercise.

While $\dot{V}O_{2max}$ is a major determinant of exercise status, the lactate threshold (LT) is regarded by many as of equal importance and this was examined in Chapter 4. The LT is operationally defined as the exercise intensity at which blood lactate accumulation begins, or an arbitrary fixed

concentration of lactate is reached during an incremental exercise test. While this concept is generally accepted, there is some disagreement with several groups suggesting that lactate increases in an exponential fashion without displaying 'threshold' behaviour. Whatever the true nature of the lactate increase during incremental exercise, the work load identified as the LT has been shown repeatedly to correlate well with endurance exercise performance and for this reason it has become a routine measurement in exercise physiology. Of the several LT measurements that were calculated in Chapter 4, each occurred at a similar percentage of $\dot{V}O_{2max}$ in CFS patients and control subjects. However, in view of the uncertainty regarding the precise pattern of lactate increase during incremental exercise, an exponential model was also used to describe the increase in plasma lactate concentration during incremental exercise. This analysis confirmed that there was no difference in the rate of increase in plasma lactate during incremental exercise. Furthermore, the collection of blood samples throughout 60 minutes of recovery also indicated that post-exercise peak plasma lactate concentration, the time to peak, and the rate of decline post-exercise in CFS patients were all similar to those in the control subjects. Given that the plasma lactate concentration at any time point during exercise is a consequence of both lactate production and lactate removal, such that a change in either or both can affect the outcome, the implication from these results is that both the production and clearance of plasma lactate are normal in CFS patients and therefore cannot contribute to their early fatigue with exercise.

While the normal values for $\dot{V}O_{2max}$ and the LT reported in CFS patients suggest that their exercise status is not impaired, the focus in such tests is on metabolic variables during exercise to exhaustion rather than sustained sub-maximal work. Yet it is exercise in this latter spectrum that most closely reflects the effort met during the activities of everyday living in sedentary individuals that is of particular concern to CFS patients. Therefore, to obtain a more complete review of exercise status, an assessment of the metabolic responses to sustained exercise was performed and the results are presented in Chapter 5. An intensity corresponding to 75% of $\dot{V}O_{2max}$ was chosen and the metabolic responses throughout 10 minutes of sustained exercise, as well as end points such as exercise duration and total work done, were examined. The metabolic responses in CFS patients of both sexes during sustained cycle ergometer exercise at ~75% of their individual values for $\dot{V}O_{2max}$ were not different from those in control subjects.

From the studies reported in this study, several conclusions can be drawn:

1. Neither maximal oxygen uptake nor any other aspect of the cardio-respiratory response to incremental exercise is different in CFS patients from that found in healthy, sedentary control subjects and cannot be contributing to their early fatigue with exercise.
2. Neither lactate production nor lactate clearance during incremental or sustained exercise was abnormal in patients with CFS and their lactate thresholds were also similar to healthy, sedentary control subjects,

together strongly implying that excess lactic acidosis cannot be a factor in their early fatigue with exercise.

3. In keeping with the results from the incremental exercise test, no aspect of the cardio-respiratory response to sustained exercise in patients with CFS was not different from that found in a group of healthy, sedentary control subjects matched for age and sex.
4. Taken together, these several findings do not support the widespread contention that exercise status is reduced in patients with CFS and, as such, cannot be contributing to their fatigue. Furthermore, these findings provide no support for the recommending GET as a means of treatment.