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Exercise lowers pain threshold in chronic fatigue syndrome

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Abstract

Post-exertional muscle pain is an important reason for disability in patients who are diagnosed to have Chronic Fatigue Syndrome (CFS). We compared changes in pain threshold in five CFS patients with five age and sex matched controls following graded exercise. Pain thresholds, measured in the skin web between thumb and index finger, *increased* in control subjects with exercise while it *decreased* in the CFS subjects. Increased perception of pain and/or fatigue after exercise may be indicative of a dysfunction of the central anti-nociceptive mechanism in CFS patients.

Keywords: Chronic fatigue syndrome; Exercise; Pain threshold

1. Introduction

Chronic Fatigue Syndrome (CFS) is a debilitating condition that is characterised by chronic fatigue, impairment of short-term memory and musculoskeletal pain (Fukuda et al., 1994). The cause of CFS is not known.

Pain is considered to be an important reason for disability in CFS. Patients with CFS experience muscle pain and post-exertional malaise following sustained exercise. The mechanism of increased muscle pain after exercise in CFS is not known but is considered to be an important reason for low compliance with graded exercise therapy (Chaudhuri, 2002).

In this study, we compared changes in pain threshold in five CFS patient with five age and sex matched control subjects following exercise. All CFS patients had been previously assessed and evaluated by one of us (AC) and fulfilled the CDC criteria for CFS (Fukuda et al., 1994). The selected patients were relatively less disabled and more functional in their daily activities.

2. Methods

The study was approved by the local ethics committee (EC/02/S/57) and informed, written consent was obtained from all subjects. All pain related treatment and anti-depressants with analgesic effects were withdrawn 48 h before testing and subjects were asked not to undertake physical exertion for 24 h prior to the investigation.

The exercise consisted of three 5-min periods on a treadmill, set to a speed of 5 km h^{-1}, with an increasing incline of 5, 10 and 15° at each stage of the graded exercise test. Pain thresholds were measured in the skin web between thumb and index finger using an Algometer designed in-house. A force is applied on both sides of the skin web with a pair of tweezers. The area of contact is 16 mm^2 and the force is measured with strain gauges. The force is gradually increased at a rate of 3 N s^{-1} until the subject indicates that the pain level has been reached. The threshold is determined as the mean of the three closest values out of five measurements. Pain thresholds were obtained before start of the exercise (baseline), immediately after each exercise period and a final pain threshold 20 min after the final exercise stage.

3. Results

Five CFS patients (median age 46 years range 28–49) and five control subjects (median age 44 years range 30–54) were studied. Each group consisted of one female and four male volunteers. Age of the participants in both groups was comparable, with the female volunteer being oldest in her

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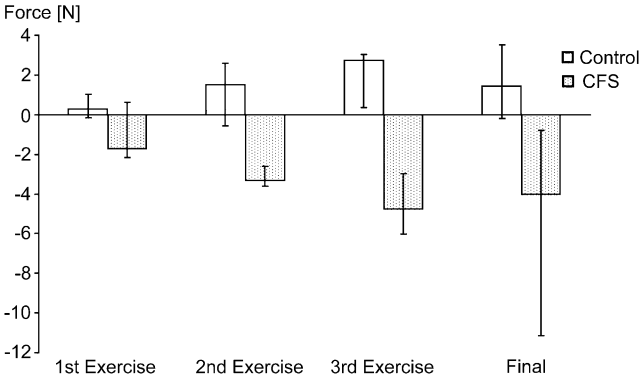

Fig. 1. Median change in pain threshold relative to baseline following graded exercise. Positive values indicate an increase and negative values a decrease in pain threshold. The error bars indicate the inter-quartile range.

respective group. All healthy volunteers and selected patients completed the exercise protocol. None of the participants, including the CFS patients, reported any muscle pain immediately after the exercise. The median baseline pain threshold was 28.6 N range 12.5–36.1 N for CFS subjects and 24.9 N range 23.9–30.3 N for controls. The influence of high inter-subject variability was reduced by analysing the changes in pain threshold from baseline values. The pain threshold increased in control subjects with exercise while it decreased in the CFS subjects as shown in Fig. 1. After the third exercise period, the median *increase* in controls of 2.7 N range −0.8 to 3.9 N was significantly different from the median *decrease* of 4.7 N range 1.1–13.3 N in CFS subjects ($P = 0.0122$, Mann–Whitney test). The difference in baseline pain threshold between the single female participants in each group was not significant. The pain threshold for the female control did not change with exercise while it was reduced in the female CFS patient.

4. Discussion

This is the first study which has looked objectively at the effect of graduated physical exercise on pain threshold in patients with CDC defined CFS. Post-exertional myalgia and chronic muscle pain have implications for successful rehabilitation programmes in CFS. Fatigue in CFS is primarily central (Chaudhuri and Behan, 2004) and none of the patients in this study had exercise induced muscle fatigability or muscle cramp to suggest a peripheral origin of fatigue.

In normal physiology, a stimulus which causes or has the potential to cause tissue damage elicits a sensation of pain by stimulating nociceptors. Different nociceptors are known to have different thresholds and nociceptors with lower thresholds may respond to pressure or heat that is not sufficient to cause tissue injury. It is considered that the low-threshold nociceptors signal impending harm and the painful sensation invoked is more of ‘warning’ rather than tissue injury. Patients with CFS experience muscle pain after a level of exertion that does not cause any tissue damage. A reduced level of beta-endorphin in the peripheral mononuclear cells of CFS patients has been observed (Panerai et al., 2002) but its clinical significance is unclear. Sex differences in responses to experimental pain have been widely reported, with men having higher pain tolerance than women (Fillingim et al., 2002). Findings from both animal and human research suggest that pain sensitivity changes across the menstrual cycle with greater ischaemic but not thermal pain sensitivity among females after the mid-cycle surge of lutenising hormone (Fillingim et al., 1997).

In our experiment, male and female CFS patients did not differ from healthy controls in terms of their pain threshold at the beginning of the exercise protocol but had a progressive decline in sensory threshold to pain after exercise. We did not observe any obvious evidence of a difference in pain threshold between the sexes but the sample size was small and unequal ($M = 4, F = 1$) for proper analysis. Despite the small number of subjects in the study, our results indicate that in comparison to the healthy controls, CFS subjects had incremental reduction in pain threshold after modest exercise. In normal circumstances, as demonstrated by our control group, exercise increases pain threshold and this is presumed to be due to the release of endogenous opioids and growth factors (Koltyn and Arbogast, 1998). Increased perception of pain and/or fatigue after exercise may be indicative of a dysfunction associated with the central anti-nociceptive mechanism. Similar observations have been made in patients with fibromyalgia where increased perception of muscle pain is considered to be due to an abnormal central nociceptive processing of the peripheral sensory input (Russell, 2002). Low serotonin (5-HT) and elevated substance P is implicated in the pain amplification syndrome in fibromyalgia (Russell, 2002). A similar mechanism may be responsible for pain amplification after exercise in CFS patients. Better understanding of the central pain mechanism in CFS would be an important step for more effective rehabilitation of the affected patients.

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