

Voluntary motor function in patients with chronic fatigue syndrome

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Abstract

Introduction: The pathogenesis of chronic fatigue syndrome (CFS) remains unknown. In particular, little is known of the involvement of the motor cortex and corticospinal system. **Methods:** Transcranial magnetic stimulation (TMS) was used to assess corticospinal function in terms of latency and threshold of motor-evoked potentials (MEPs) in thenar muscles. Reaction times and speed of movement were assessed using button presses in response to auditory tones. **Results:** Patients had higher ($P < .05$) self-assessed indices of fatigue (7/10) than for pain (5/10), anxiety (4/10) or depression (3/10). Mean (\pm S.E.M.) simple reaction times (SRTs) were longer ($P < .05$) in the patients (275 ± 19 ms) than in the controls (219 ± 9 ms); choice reaction times (CRTs) were not significantly longer in the patients. Movement times, once a reaction task had been initiated, were

longer ($P < .05$) in the patients in both SRTs (patients, 248 ± 13 ms; controls, 174 ± 9 ms) and CRTs (patients, 269 ± 13 ms; controls, 206 ± 12 ms). There was no difference ($P > .05$) in threshold or latency of MEPs in hand muscles between the patients (threshold, $54.5 \pm 2.2\%$ maximum stimulator output [%MSO]; latency 22 ± 0.3 ms) and controls (threshold $54.6 \pm 3.6\%$ MSO; latency 22.9 ± 0.5 ms). Regression analysis showed no correlation ($P > .05$) of SRTs with either threshold for MEPs or fatigue index. **Conclusion:** Corticospinal conduction times and excitability were within the normal range despite a slower performance time for motor tasks and an increased feeling of fatigue. This suggests that the feeling of fatigue and the slowness of movement seen in CFS are manifest outside the corticospinal system. © 2001 Elsevier Science Inc. All rights reserved.

Keywords: Chronic fatigue syndrome (CFS); Corticospinal; Electromyography (EMG); Reaction time; Transcranial magnetic stimulation (TMS)

Introduction

Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME), is characterized by the feeling of fatigue, musculoskeletal pain and many neuropsychiatric symptoms [1]. The pathogenesis of CFS remains unknown, although it does appear to be associated with neuroendocrine [2] and immunological abnormalities [3].

A number of studies have measured reaction times in CFS and have reported them to be slowed [4–7]; however,

they have not all differentiated between choice and simple reaction time (SRT) paradigms.

One previous study that investigated corticospinal function in CFS showed increased facilitation of motor-evoked potential (MEP) to transcranial magnetic stimulation (TMS) of the motor cortex [8] after exercise. Others have shown that the excitability of the motor cortex is unstable in CFS during sustained muscle activity [9] and speculated that this might exaggerate the perception of fatigue.

In the present study, our hypothesis was that altered corticospinal function might, at least in part, be responsible for the genesis of fatigue. To test this, we have measured simple and choice reaction times (CRTs), electrophysiological indices of corticospinal function and self-assessment ratings of symptoms.

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Methods

Patients and control subjects

Following local ethical approval from the Riverside Research Ethics Committee and the St. Mary's Hospital Research Ethics Committee, 13 patients (aged 26–62 years; two left-handed; six men, seven women) with CFS were recruited from the general medicine clinic at St. Charles Hospital, London. The patients, diagnosed according to the criteria described by Fukuda et al. [10], were investigated by a general physician and a psychiatrist in order to exclude other medical or psychiatric disorders that may be responsible for the symptoms. The patients were compared with 10 healthy control subjects (aged 21–51 years; two left-handed; six men, four women), recruited mostly from hospital and medical school staff with no known medical or psychiatric disorder. A power calculation, using this number of individuals, gave the study a power of greater than 0.9. The duration of CFS symptoms in the patients ranged from less than a year to 14 years. Nine patients were taking medication: low-dose antidepressants ($n=6$), homeopathic medicines ($n=1$), vitamins ($n=3$), or food supplements ($n=2$). All abstained for at least 3 days before the study.

Patient self-assessment

Each patient completed a self-assessment of the prevailing symptoms on the day of the tests. Patients were asked to mark a vertical tick somewhere on a 10-cm line to indicate the severity of the following symptoms: actual pain experienced, impact of pain on life, fatigue, anxiety, and depression.

Measurement of reaction times

All subjects performed trials to assess SRT, CRT, and their speed of movement once they had reacted in both the SRT (simple movement time, SMT) and CRT (choice movement time, CMT) tasks. Subjects used their dominant hand to perform the reaction time testing. An in-house computer program running on an IBM-compatible PC was used to measure reaction and movement times. Subjects were seated comfortably at a table on which were three buttons placed 15 cm apart.

In the SRT task, the subject depressed the center button (Button-1) and after a randomized delay (1–3 s), a tone sounded and the subject released Button-1 as quickly as possible and depressed Button-2 on the contralateral side to the hand used. SRT was measured as the time between the tone and release of Button-1 and SMT the time between release of Button-1 and depressing Button-2. In the CRT, high or low tones were sounded at random in each trial. If the low tone sounded, then subjects were instructed to release Button-1 and depress Button-2 as in the SRT. If a

high tone sounded, subjects were instructed to release Button-1 and depress Button-3 located on the ipsilateral side to the hand used. In both tasks, subjects were given 10 practice trials and then completed 50 experimental trials.

Reaction times of less than 100 ms or greater than 500 ms were excluded as either anticipations or mistakes. Mean reaction times and movement times were calculated for each individual.

Assessment of corticospinal pathways

Electromyographic (EMG) recordings were made from the thenar muscles of the dominant hand using self-adhesive surface electrodes (Arbo Neonatal Pink). The EMG signal was amplified $1000 \times$ (World Precision Instruments, Iso-Dam) and filtered (± 3 dB) below 100 Hz and above 2000 Hz. The sensitivity of a visual feedback system was set so that subject could maintain a contraction of approximately 10% maximum voluntary contraction (MVC) or remain relaxed. EMG data was sampled (4000 Hz) using an analogue-to-digital computer interface (Cambridge Electronic Design 1401 and IBM-compatible PC) and signal averaging software (SIGAVG).

TMS of the motor cortex was delivered using a MagStim 200 stimulator connected to a 9-cm circular stimulating coil centered over the vertex. The stimulus intensity was adjusted in steps equivalent to 1% of the maximum stimulator output (MSO) and 10 stimuli were delivered at each strength. Threshold TMS for producing a MEP was defined as that lowest strength that elicited MEPs on more than half the presentations. MEPs were rectified and averaged. Threshold and latency of MEPs were assessed with the thenar muscles relaxed and during an isometric contraction of 10% MVC.

Statistics

Self-rated patient indices were compared using one-way ANOVA with Bonferroni correction. Reaction times, movement times, threshold, and latency of MEPs were compared between patients and controls using one-way ANOVA. Pearson product–moment correlation was used to look for correlation between MEP thresholds and SRTs or self-rated indices of fatigue. Results were taken as statistically significant when $P < .05$.

Results

Patient self-assessment

The mean (\pm S.E.) self-rated index for fatigue (7.0 ± 0.4) was higher ($F=4.23$; $P < .05$) than those for pain (4.3 ± 0.8), impact of pain (4.6 ± 1.1), anxiety (3.7 ± 0.7), or depression (3.3 ± 0.6). There was no statistical difference between any other of the symptoms assessed.

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