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Capturing the post-exertional exacerbation of fatigue following physical and cognitive challenge in patients with chronic fatigue syndrome

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ABSTRACT

Objective: To design and validate an instrument to capture the characteristic post-exertional exacerbation of fatigue in patients with chronic fatigue syndrome (CFS).
Methods: Firstly, patients with CFS (N = 19) participated in five focus group discussions to jointly explore the nature of fatigue and dynamic changes after activity, and inform development of a self-report instrument — the Fatigue and Energy Scale (FES). The psychometric properties of the FES were then examined in two case–control challenge studies: a physically-demanding challenge (moderate-intensity aerobic exercise; N = 10 patients), and a cognitively-demanding challenge (simulated driving; N = 11 patients). Finally, ecological validity was evaluated by recording in association with tasks of daily living (N = 9).
Results: Common descriptors for fatigue included 'exhaustion', 'tiredness', 'drained of energy', 'heaviness in the limbs', and 'foggy in the head'. Based on the qualitative data, fatigue was conceptualised as consisting of 'physical' and 'cognitive' dimensions. Analysis of the psychometric properties of the FES showed good sensitivity to the changing symptoms during a post-exertional exacerbation of fatigue following both physical exercise and driving simulation challenges, as well as tasks of daily living.
Conclusion: The 'fatigue' experienced by patients with CFS covers both physical and cognitive components. The FES captured the phenomenon of a post-exertional exacerbation of fatigue commonly reported by patients with CFS. The characteristics of the symptom response to physical and cognitive challenges were similar. Both the FES and the challenge paradigms offer key tools to reliably investigate biological correlates of the dynamic changes in fatigue.

Introduction

Chronic fatigue syndrome (CFS) is a complex and debilitating medical condition. The international consensus diagnostic criteria for the syndrome stipulate that the fatigue is not relieved by rest; is present for at least 6 months; and co-occurs with at least four of eight additional symptoms, such as muscle or joint pain, unrefreshing sleep, and difficulties with memory or concentration [1]. CFS is also characterised by a prolonged exacerbation of symptoms induced by activity, commonly termed 'post-exertional malaise', or colloquially by patients as a 'crash' or 'bust'. Recently devised sets of diagnostic criteria emphasise the importance of the post-exertional exacerbation of fatigue and symptoms in the diagnosis of CFS [2,3]. The exacerbation of symptoms is commonly reported after both physical and cognitive activities [4]; however, the phenomenon is not well understood and has not been well characterised experimentally [5].

Many self-report instruments have been designed to record this symptom in patients with CFS (reviewed in [6–8]). The vast majority of the existing self-report instruments have been designed to capture the state in a retrospective, period prevalence format — e.g. "In the past week have you…?" However, to accurately characterise the 'post-exertional malaise' phenomenon in CFS (i.e. the change in severity and nature of this symptom following strenuous activity, and the time-course of recovery), the scale needs to be able to detect dynamic changes in fatigue over short time periods. The most common tool currently used to measure fatigue in real-time has been a simple, single variable, visual analogue scale (VAS), which allows a uni-dimensional characterisation of the severity of a symptom. Importantly, previous attempts to conceptualise the fatigue experienced by patients with CFS have highlighted the multi-dimensionality of the sensation [9–14].

The overall aim of the studies reported here was to develop reproducible challenge protocols to investigate biological correlates of the

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post-exertional exacerbation of fatigue in patients with CFS. Specifically, the aims were as follows: firstly, to utilise mixed methods to design and test a brief questionnaire to characterise the fatigue state, including during exacerbation; and secondly, to develop physical and cognitive challenge protocols to allow study of the post-exertional exacerbation of fatigue; and thirdly, to assess the ecological validity on the questionnaire in real world 'challenge' settings.

Methods

Overview

Focus groups were utilised to characterise the phenomena of fatigue in patients with CFS, from which a self-report instrument — the Fatigue and Energy Scale (FES), was devised. Protocols were developed for an aerobic exercise challenge (termed here EXER), and a cognitively-demanding challenge (termed here COG) and assessed in separate case–control studies. Data from objective measures assessed in these challenge studies will be presented in supporting papers. Ecological validity of the FES was assessed by evaluation of patient recordings during varied tasks of daily living. All patients were diagnosed with CFS by a specialist physician according to the consensus international diagnostic criteria [1], and were recruited from those attending the Fatigue Clinic, University of New South Wales, in Sydney, Australia for management of CFS via a 12-week outpatient treatment programme incorporating cognitive–behavioural therapy, activity pacing and graded exercise therapy. Each study was approved by the institutional Human Research Ethics Committee. All participants provided informed, written consent.

Focus groups

Participants

Nineteen patients (84% female; mean age was 33 ± 7 years) participated in the focus groups. The mean illness duration was 5.5 ± 4.0 years (range 1.0–10.0). All participants reported significant disability (SF-36 scale [15]: mean physical role functioning score 51 ± 18; mean mental health score 59 ± 22). The majority of the group (17; 89%) were able to complete activities of daily living, and four participants were managing full-time or part-time study or employment despite ongoing illness. Five participants (26%) were receiving a sickness allowance or disability support. All participants had completed secondary schooling, and a majority (10; 58%) had earned a university degree or higher.

Design

A focus group forum was chosen to allow participants to compare and contrast their experiences, generating a comprehensive list of descriptors. In the days before the discussion, participants were asked to note down descriptors for the 'fatigue' and related symptoms they experienced at different times of the day that captured both the nature of the phenomenon and its severity. The sessions were led by the same trained moderator, and lasted 30 to 60 min with rest breaks.

Discussions were semi-structured with a list of open-ended questions asked (Appendix A). Participants were encouraged to describe their experiences of the illness, and specifically the feelings of 'fatigue', including comparison with pre-illness. The open-ended prompts sought to cover the dimensionality of this feeling based on similar research in other fatigue-related disorders [16–18], and also explored changes in the feeling of 'fatigue' during and after physical, mental or emotional challenges. Queries to prompt discussion of the comparison between 'fatigue' with the feelings of sleepiness or low mood were introduced only when a participant mentioned these topics. The moderator actively led the discussion only when the topic moved away from the nature of 'fatigue'. At the conclusion of each group, the moderator listed the key descriptors and invited further clarification or disagreement.

Transcript analysis

Each focus group was audiotaped, transcribed verbatim and analysed using NVivo software (ver. 9.2 QSR International, Doncaster, Australia). Numbers were allocated to each focus group and participant in the transcripts to preserve anonymity. Focus groups were conducted until 'saturation' (i.e. no new themes/descriptors identified). Transcripts were reviewed and analysed by AK and BB. Coding was used to identify general themes and descriptors; and word count analysis to quantify the number of times a specific descriptor was used. After the first pass reading of the transcripts, themes were compared and contrasted until consensus was reached and a preliminary list of descriptors was formed (e.g. 'heavy'). After the second pass, the code frame for each descriptor was further refined (e.g. 'heaviness in the limbs or body'). A word frequency count for each of the key descriptors was performed, and checked for validity during the third reading by analysing the context of each descriptor's use accounting for any instances where the descriptor was used by the moderator, or used multiple times within a participant's response. Synonyms for each descriptor were included in the word frequency analysis, but analogies, metaphors and similes were not included. Frequently-used terms deemed to be describing independent symptoms (e.g. 'painful', 'sleepy', and 'aching') or functional impact (e.g. 'unable to think') were also excluded from the frequency analysis.

Based on this process, a self-report instrument was designed to capture these features. Key descriptive themes drawn from the data were used to develop fatigue dimensions (e.g. physical fatigue and mental fatigue), and domains within each dimension (general fatigue; loss of energy; and function).

Laboratory challenge studies

Participants

Patients with CFS (EXER: N = 10; COG: N = 11) were recruited from those attending a specialised tertiary clinic for management of patients with CFS diagnosed according to the international criteria [1]. Participants in the EXER and COG studies were approached only after the treating clinicians had resolved that they had a stable pattern of symptoms, and optimised sleep-wake cycle patterns and mood profiles, to minimise confounding influences on the fatigue experience. For the EXER study, patients were selected on the basis that their treating clinicians resolved that the patients I) were completing clinician-programmed regular low-intensity exercise (e.g. approximately 10 min walking at a gentle pace without inducing an exacerbation of symptoms); II) were not taking agents known to affect the autonomic nervous system (e.g. beta-blockers), hypothalamic–pituitary axis (HPA; e.g. fludrocortisone), or cytokine activity (e.g. prednisone); and III) had no other contraindication to participation (e.g. untreated anxiety and cardiovascular complaints). For the COG study, patients were selected on the basis that their treating clinicians resolved that the patients I) reported significant cognitive symptoms, such as the report of 'brain fog' or difficulties with short term memory or concentration; II) gave a history of worsened symptoms following cognitive activity; and III) were capable of performing a driving simulation task and computer-based assessment for at least 30 min. All participants were non-smokers.

Healthy control participants (EXER: N = 12; COG: N = 11) were recruited by advertisement from university staff and students. Controls were matched by age, sex, BMI and self-reported levels of physical activity per week (typical hours per week of at least moderate intensity exercise).

Design

Study protocols involved multiple assessments using the FES before and after each challenge. Baseline assessments were conducted 24 h prior, and immediately prior, to the challenge. Post-challenge assessments were conducted immediately following challenge (post-0) and