Efficacy of cognitive behavioral therapy for chronic fatigue syndrome: a meta-analysis
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CRD summary
This review evaluated the efficacy of cognitive behavioural therapy (CBT) in chronic fatigue syndrome. The authors concluded that CBT had a moderate positive effect. Inadequate information about participants and interventions, lack of reporting of study quality and differences between studies meant that it was difficult to assess the reliability of the authors' conclusions.

Authors' objectives
To evaluate the efficacy of cognitive behavioural therapy (CBT) in patients with chronic fatigue syndrome (CFS).

Searching
PubMed and PsycINFO were searched from inception to June 2007 using reported search terms. In addition, reference lists of relevant articles were screened and corresponding authors contacted for details of any unpublished studies.

Study selection
Randomised controlled trials (RCTs) that compared interventions with a cognitive and/or behavioural emphasis with a control treatment (waiting list, usual treatment of an intervention that would not be expected to be helpful) in patients with chronic fatigue or CFS were eligible for inclusion. The review also included studies that compared CBT with credible control treatment. Studies had to assess measures of chronic fatigue including self-report measures of physical and mental fatigue, subjective and objective measures of everyday and cognitive functioning. The review did not assess depression or anxiety.

Most of the included studies evaluated interventions that included cognitive treatment; the other studies evaluated activity with no cognitive treatment. In the review all experimental interventions were referred to as CBT. Most studies compared the experimental intervention with waiting list, usual treatment, simple advice or no treatment; other studies used a credible control treatment. All but one of the included studies evaluated individual treatment. All studies encouraged a gradual increase in activity. No other details of interventions were reported. Most studies diagnosed patients using the Oxford or Centres for Disease Control (1994) criteria. The authors stated that only one study exclusively involved adolescents. Studies generally used multiple outcome measures. The review assessed changes in fatigue levels and the proportion of CBT patients who were within the normal fatigue range at latest follow-up. The duration of follow-up ranged from three to 14 months.

The authors stated neither how papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Two reviewers independently assessed quality using the 12-item scale of Burke, Arkowitz and Menchola. Disagreements were resolved through discussion. Items assessed included use of objective outcome measures and blinding of outcome assessors.

Data extraction
Two reviewers independently extracted and coded data. Disagreements were resolved by consensus. Authors were contacted for missing data if required. For each study, means and standard deviations were extracted and used to calculate separate effect sizes for each category of outcome variable for the longest follow-up period. Effect sizes (g) were adjusted for small sample sizes to produce an unbiased estimate. A mean effect size was calculated for all relevant outcome variables in individual studies. Separate effect sizes were calculated for each comparison within individual studies. Effect sizes from one study that were identified as outliers were reduced to the closest relevant non-outlier values in that study.

Methods of synthesis
Mean difference effect sizes (ES) were pooled using inverse variance methods. Heterogeneity was assessed using the Q statistic. The number of studies required to nullify any statistically significant finding for the main analysis (Fail-safe N) was also estimated.

Univariate analysis was used to examine the influence of the following potential modifying variables: type of fatigue (physical or mental); methods used to measure fatigue (objective or other); inclusion of encouragement to gradually increase activity; use of credible control group; diagnostic criteria; number of treatment hours and sessions; duration of follow-up; and study quality.

**Results of the review**

Thirteen RCTs were included (n=1,371).

CBT interventions were associated with a statistically significant and moderate reduction in fatigue compared to controls: ES 0.48 (95% CI: 0.27, 0.69, p<0.001). Significant heterogeneity was found (p<0.001). Fail-safe N=57. The mean CBT drop-out rate was 12 per cent. The CBT drop-out rate at the latest follow-up was reported in the abstract of the paper as ranging from 33 per cent to 73 per cent.

CBT interventions were associated with a greater effect size for physical compared to mental fatigue: ES =0.81 (95% CI: 0.50, 1.11, p<0.001) for physical fatigue and 0.20 (95% CI: -0.20, 0.59, p=0.325) for mental fatigue.

The proportion of CBT patients who were within the normal fatigue range at latest follow-up ranged from 33 per cent to 73 per cent across five studies (unweighted average 50 per cent).

No statistically significant modifying variables were found.

**Authors’ conclusions**

CBT had a moderate positive effect on patients with CFS.

**CRD commentary**

The review question was clearly stated and indicated that CBT was to be the focus of the review. Inclusion criteria were specified for study design, intervention, control and participants, and apparently indicated that cognitive or behavioural interventions were to be compared to a non credible control. Some experimental interventions did not include cognitive treatment and some controls were credible treatments. Thus, it appeared that inclusion criteria were not adhered to and inclusion criteria did not appear to reflect the stated review aim. Two relevant databases were searched and authors were contacted, but it was not clear if attempts were made to minimise language bias. Methods were used to minimise reviewer errors and bias in the assessment of validity and extraction of data, but it was not clear whether similar steps were taken in study selection. The authors stated that validity was assessed, but results were not reported and so it was not possible to comment on the reliability of the results presented.

Other than diagnostic criteria, no information was provided about participants. In addition, very few details were provided about interventions and no information was given about measures used to assess outcomes, so it was not possible to determine the clinical heterogeneity among studies and hence the appropriateness of pooling data. Reducing apparently outlier effect sizes in one study to the closest relevant non-outlier values in that study appeared questionable.

Data were pooled using meta-analysis and significant statistical heterogeneity was found. Various potential sources of heterogeneity were examined and some potential reasons for differences between studies were discussed. Inadequate information about participants and interventions, lack of reporting of study quality and differences between studies meant that it was difficult to assess the reliability of the authors’ conclusions.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors suggested that future research should investigate the effect of the following for patients with
CFS: effect of number of hours of CBT treatment; effect of encouragement to increase mental activity in addition to CBT; methods to reduce drop-outs; interventions to increase the proportion of patients who moved into and remain in the normal range for fatigue measures; and whether the outcome varied with diagnostic criteria used. Future studies should adequately describe interventions and present an effect size (preferably Cohen's d) for each outcome variable together with the number of patients in each treatment group who move into the normal range for fatigue measures.

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