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Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial

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Abstract

Objective To evaluate the efficacy of cognitive behaviour therapy for adolescents aged 10-17 years with chronic fatigue syndrome.
Design Randomised controlled trial.
Setting Department of child psychology.
Participants 71 consecutively referred patients with chronic fatigue syndrome; 36 were randomly assigned to immediate cognitive behaviour therapy and 35 to the waiting list for therapy.
Intervention 10 sessions of therapy over five months. Treatment protocols depended on the type of activity pattern (relatively active or passive). All participants were assessed again after five months.
Main outcome measures Fatigue severity (checklist individual strength), functional impairment (SF-36 physical functioning), and school attendance.
Results 62 patients had complete data at five months (29 in the immediate therapy group and 33 on the waiting list). Patients in the therapy group reported significantly greater decrease in fatigue severity (difference in decrease on checklist individual strength was 14.5, 95% confidence interval 7.4 to 21.6) and functional impairment (difference in increase on SF-36 physical functioning was 17.3, 6.2 to 28.4) and their attendance at school increased significantly (difference in increase in percentage school attendance was 18.2, 0.8 to 35.5). They also reported a significant reduction in several accompanying symptoms. Self reported improvement was largest in the therapy group.
Conclusion Cognitive behaviour therapy is an effective treatment for chronic fatigue syndrome in adolescents.

Introduction

Patients with chronic fatigue syndrome have debilitating unexplained severe fatigue that is not the result of an organic disease or ongoing exertion and is not alleviated by rest. Symptoms last for at least six months and are accompanied by other symptoms like muscle pain and unrefreshing sleep.[1 2] This condition can occur in adults and adolescents.[3] Several randomised controlled trials have shown that cognitive behaviour therapy is effective in adults.[4 5] To date, however, there have been no published controlled studies on such therapy for adolescents, though one uncontrolled study suggested that such a behavioural approach can reduce fatigue in adolescents.[6] Development of potentially effective interventions is especially important in young people to avoid prolonged absence from school and restricted social activities, which threaten healthy development.[7–9]

Methods

We studied the efficacy of cognitive behaviour therapy for adolescents with chronic fatigue syndrome by comparing outcome in those randomly assigned to immediate therapy with outcome in those who were assigned to the waiting list for therapy. We used two treatment protocols: one for patients with a passive physical activity pattern and one for relatively active patients.[4 10 11] We hypothesised that fatigue severity, functional impairment, and school absence would decrease significantly more in those assigned to immediate therapy.

Patients

As part of the usual care all consecutive patients with a major complaint of fatigue referred to the paediatrics outpatient clinic between October 1999 and October 2002 were assessed by means of a detailed history and physical and laboratory examinations. Patients were eligible if they were between 10 and 17.2 years of age (to allow the older participants to complete therapy before their 18th birthday) and met the US Centers for Disease Control Prevention criteria for chronic fatigue syndrome.[1] Severe fatigue and severe functional impairment were defined as scores of 40 or more on the fatigue severity subscale of the checklist individual

ELPS *This is the abridged version of an article that was posted on bmj.com on 14 December 2004: http://bmj.com/cgi/doi/10.1136/bmj.38301.587106.63*

strength[4] and a weighted score of 65 or less on the SF-36 physical functioning subscale. We excluded patients with psychiatric comorbidity, as assessed during an interview with both patients and parents by an experienced child psychologist before randomisation.

Design and procedures

We gave patients and their parents verbal and written information about the study and obtained informed consent before randomisation. Before baseline assessments, patients were randomly allocated to one of the two groups by means of a sequence of labelled cards contained in sealed numbered envelopes that were prepared by a statistical adviser and opened by the researcher in the presence of patient and parent(s).

Patients assigned to immediate therapy had to agree to not having any further medical examinations or other treatments for fatigue during therapy.[4] Patients assigned to the waiting list were assessed directly after randomisation and five months later. No further requirements were made during the waiting period, and they were free to have other examinations or treatments. They were informed beforehand that, if desired, they could start therapy directly after the second assessment.

Intervention

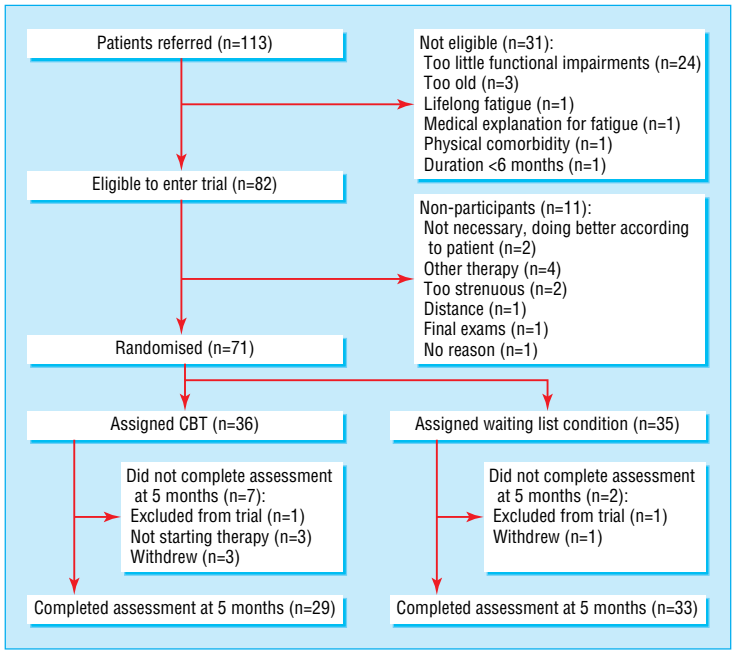
The therapy comprised 10 individual sessions over five months. Four child therapists who were trained and supervised by an experienced cognitive behavioural therapist administered all therapy. We used two treatment protocols based on the existing protocols for adults and adapted for the two types of patterns of physical activity.[4 11] Adolescents with a relatively active physical activity pattern alternate between periods of activity and periods of rest.[11] In contrast, those with a passive physical activity pattern spend most time lying down and go out infrequently. Most do not attend school at all.

Active patients—For relatively active patients treatment started with them learning to recognise and accept their current state of fatigue and impairment. Subsequently, they reduced their levels of activity and learnt to respect the limitations. After achieving this balance, the patient started to build up activity levels. This protocol was used in the trial of Prins et al.[4]

Passive patients—For passive patients we started a systematic programme of activity building as soon as possible. To assure adherence, we first addressed and challenged their beliefs that activity would aggravate symptoms. In such patients it is thought to be counterproductive to reduce activity levels any further or reinforce the patient's need to respect limitations.[11]

Primary outcome variables

We measured fatigue with the fatigue severity subscale of the checklist individual strength, a questionnaire originally developed for adults.[4 12 13] We measured functional impairment with the "physical functioning" subscale of the SF-36 (range 0 (maximum physical limitations) to 100 (ability to do vigorous activity)). School attendance was calculated by dividing the hours that the patient attended lessons in the previous week by the hours that the patient should have attended.



Trial profile

Analysis

Power calculations showed that we needed 30 patients in each group to achieve 90% power to detect a difference of 7 points on the fatigue severity subscale with an $\alpha < 5\%$ (two tailed).[14] We used SPSS (version 10.0) for all statistical analyses. We analysed data on an intention to treat basis and carried forward last observations in cases of missing data. Differences between groups on the amount of change in the primary outcome variables were calculated with analyses of variance on differences in scores before and after the five months, with 95% confidence intervals.

Results

The figure shows the trial profile. Seventy one patients were randomly allocated either to immediate therapy (n=36) or to remain on the waiting list (n=35). After randomisation we excluded two patients (one from each group) because the diagnosis of chronic fatigue syndrome was incorrect. Analyses were based on the 69 remaining patients. Of those, 29 in the immediate

Table 1 Baseline characteristics of study participants. Values are means (SD) unless stated otherwise

	Cognitive behaviour therapy (n=35)	Waiting list (n=34)
Demography		
Age (years)	15.6 (1.3)	15.7 (1.3)
Median duration of complaints (months)	16.0	18.0
No (%) female	31/35 (89)	31/34 (91)
Primary outcome variables		
Fatigue severity (checklist individual strength)	52.5 (3.8)	51.6 (4.3)
Physical functioning (SF-36)	42.1 (16.5)	45.3 (17.0)
No (%) with school attendance:		
Full	4/35 (11)	6/34 (18)
Partial	31/35 (89)	28/34 (82)
Physical activity pattern (No (%))		
Pervasively passive	10/33* (30)	7/34 (21)
Relatively active	23/33* (70)	27/34 (79)

*Two participants refused to wear an actometer.

Table 2 Effect of cognitive behaviour therapy on fatigue severity, functional impairment, and school attendance

Condition*	Mean score (SD)		Treatment effect† (95% CI)	P value
	0 months	5 months		
Fatigue severity				
Cognitive behaviour	52.5 (3.8)	30.2 (16.8)	14.5 (7.4 to 21.6)	0.001
Waiting list	51.6 (4.4)	44.0 (13.4)		
Physical functioning				
Cognitive behaviour	42.1 (16.5)	69.4 (28.0)	17.3 (6.2 to 28.4)	0.003
Waiting list	45.3 (17.0)	55.3 (21.1)		
School attendance				
Cognitive behaviour‡	46.2 (38.9)	74.7 (37.8)	18.2 (0.8 to 35.5)	0.040
Waiting list	56.4 (38.6)	66.7 (36.0)		

*Cognitive behaviour therapy n=35; waiting list n=34.
†Difference in improvement between intervention and control group.
‡Two participants were left out of analyses because they had taken their final examinations and therefore were not required to attend school at five months.

therapy group and 33 from the waiting list completed the assessment at five months. Six patients dropped out during the course of treatment, three of them did not finish the second assessment. Table 1 shows the baseline characteristics of both groups.

Effect of intervention

Primary outcome—Patients in the immediate therapy group reported a significantly greater decrease in fatigue severity (difference in decrease on checklist individual strength 14.5, 95% confidence interval 7.4 to 21.6) and functional impairment (difference in increase on SF-36 physical functioning 17.3, 6.2 to 28.4) than patients on the waiting list. School attendance also increased significantly more in the therapy group (difference in increase in school attendance 18.2, 0.8 to 35.5) (table 2).

Two treatment protocols—There were no statistically significant differences in all primary outcomes between adolescents who were treated with the protocol designed for patients with a passive physical activity pattern and those who were treated with the protocol for more active patients. For further details of secondary analyses and secondary outcomes see the long version of this paper on bmj.com.

Discussion

In adolescents with chronic fatigue, cognitive behaviour therapy was more effective than remaining on a waiting list in reducing severity of fatigue, improving physical functioning, and increasing school attendance. These results endorse the findings of previous studies on the efficacy of cognitive behaviour therapy for adults with chronic fatigue syndrome.[4 5] Passive and active patients showed equal improvements on all primary outcome variables. Furthermore, rates of improvement were larger than seen in the study by Prins et al, in which only one protocol was used to treat all patients.[4]

We tried to maximise inclusion by repeatedly informing general practitioners and paediatricians about the study and prolonging recruitment. Nevertheless, our final samples were still relatively small. This may be due to underdiagnosis because of unfamiliarity with adolescent chronic fatigue syndrome or may point to reluctance of doctors to diagnose this syndrome. Alternatively, chronic fatigue syndrome may be less common than previously estimated.[3] We believe that our results can be generalised to other adolescents who fulfil the diagnostic criteria for chronic fatigue syndrome as our patients were referred from a large part of the Netherlands.

Six patients (19%) withdrew from therapy. Most withdrawals occurred in the first half of the study, suggesting that therapists became more experienced in meeting the specific need for enhancing motivation of adolescent patients. As we did not have reference scores for activity pattern in adolescents, we used scores for adults. Fortunately, our results showed that mean activity levels and distributions of types of activity were similar to those in adults. Thus the use of reference scores for adults should not have led to misclassification.

Almost 60% of the patients in the immediate therapy group returned to full time education, an important indication of recovery. The prevalence of additional symptoms decreased significantly in the immediate treatment group. Nevertheless, as in a previous report,[15] many young people in both groups continued to report additional symptoms. Apparently, a complete resolution of additional symptoms is not a requirement of recovery, as has been suggested before.[16]

This study is the first randomised controlled trial to show that cognitive behaviour therapy can successfully be used to treat adolescents with chronic fatigue syndrome.

What is already known on this topic

Cognitive behaviour therapy is an effective treatment for chronic fatigue syndrome in adults, and one uncontrolled study has shown that it can reduce fatigue in adolescents

Chronic fatigue syndrome in adolescents can affect normal development

What this study adds

A cognitive behaviour therapy programme based on gradually increasing activity and challenging perpetuating beliefs helped adolescents with chronic fatigue syndrome

Relatively active patients as well as those with a passive physical activity pattern benefited from tailored therapy

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Insulin resistance and depression: cross sectional study

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A recent study found that depression is inversely associated with insulin resistance, but positively associated with diabetes.[1] Association between insulin resistance and depression is a poorly studied area and the few earlier findings do not necessarily support this finding,[1] indicating that patients with serious depression have insulin resistance assessed by insulin tolerance, intravenous, or oral glucose tolerance tests.[2] Recently, depression was found to be associated with greater insulin resistance in women with polycystic ovary syndrome.[3] Also, more than the normal rates of depression had already been noted in patients with clinically manifest diabetes.[2] Since insulin resistance is positively associated with the development of diabetes,[1] we hypothesised—given that disturbed glucoregulatory functions behind the development of diabetes might be associated with pathophysiological changes in depression[2]—that insulin resistance should be positively correlated with depressive symptoms. We also investigated whether depressive symptoms varied with different levels of a disturbed glucose metabolism.

What is already known on this topic

More than normal rates of depression can already be detected in patients with clinically manifest diabetes

The association between insulin resistance and depression is a sparsely studied area, and the few existing findings are contradictory

What this study adds

A positive correlation between insulin resistance and severity of depressive symptoms is present already in subjects with impaired glucose tolerance before the outbreak of type 2 diabetes mellitus

Participants, methods, and results

We invited all 1008 people born in 1935 and living in the city of Oulu, Finland, on 1 October 1990 to participate in a study to assess the prevalence of type 2 diabetes and impaired glucose tolerance; 831 attended. The follow up of the earlier participants, on which this study was based (n = 593), was done in 1996-1998; we excluded patients previously diagnosed as having diabetes, leaving 491 cases. A detailed description of the data was given earlier.[4] We defined insulin resistance with the qualitative insulin sensitivity check index,[4] and we evaluated the severity of depressive symptoms with Beck's depression inventory 21.[5] We found a negative correlation between the scores (Spearman correlation coefficient $r = -0.13$, $P = 0.004$). The correlation (see figure on bmj.com) was most evident in subjects with impaired glucose tolerance ($r = -0.24$, $P = 0.029$; table). Regarding

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P+ *A figure showing the results is on bmj.com*

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