Regular Article

Psychotherapy and Psychosomatics

Psychother Psychosom 2007;76:171–176
DOI: 10.1159/000099844

Is a Full Recovery Possible after Cognitive Behavioural Therapy for Chronic Fatigue Syndrome?

Hans Knoop[a] Gijs Bleijenberg[a] Marieke F.M. Gielissen[a]
Jos W.M. van der Meer[b] Peter D. White[c]

[a]Expert Centre Chronic Fatigue and [b]Department of Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; [c]Department of Psychological Medicine, Barts and the London Queen Mary School of Medicine and Dentistry, London, UK

Key Words
Chronic fatigue syndrome, recovery · Cognitive behavioural therapy, outcome

Abstract
Background: Cognitive behavioural therapy (CBT) for chronic fatigue syndrome (CFS) leads to a decrease in symptoms and disabilities. There is controversy about the nature of the change following treatment; some suggest that patients improve by learning to adapt to a chronic condition, others think that recovery is possible. The objective of this study was to find out whether recovery from CFS is possible after CBT. ***Methods:*** The outcome of a cohort of 96 patients treated for CFS with CBT was studied. The definition of recovery was based on the absence of the criteria for CFS set up by the Center for Disease Control (CDC), but also took into account the perception of the patients' fatigue and their own health. Data from healthy population norms were used in calculating conservative thresholds for recovery. ***Results:*** After treatment, 69% of the patients no longer met the CDC criteria for CFS. The percentage of recovered patients depended on the criteria used for recovery. Using the most comprehensive definition of recovery, 23% of the patients fully recovered. Fewer patients with a co-morbid medical condition recovered. ***Conclusion:*** Significant improvement following CBT is probable and a full recovery is possible. Sharing this information with patients can raise the expectations of the treatment, which may enhance outcomes without raising false hopes.

Introduction

Between 50 and 70% of the patients show a significant reduction of symptoms and disabilities after cognitive behavioural therapy (CBT) for chronic fatigue syndrome (CFS) [1, 2]. The nature of this improvement is uncertain. Some suggest that patients improve by adapting better to a chronic condition, while others think that recovery is possible [3]. This debate shows some similarities to the issue of recovery from mood disorders [4, 5].

The attitude of the therapist towards the treatment goals will affect the expectations and perceptions of the patient. If learning to cope with CFS is the jointly agreed maximal goal of treatment, patients will engage with treatment accordingly. If the therapist suggests that recovery is possible, the patient expectations are raised, which in turn may lead to a change in the perception of symptoms as well as disability. This is also the essence of the placebo response. The placebo response of CFS patients to psychological interventions is lower than that related to biomedical interventions and lower than that

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0033–3190/07/0763–0171$23.50/0

Accessible online at:
www.karger.com/pps

H. Knoop
Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre
POB 9011
NL–6525 EC Nijmegen (The Netherlands)
Tel. +31 243 610 030, Fax +31 243 610 041, E-Mail j.knoop@nkcv.umcn.nl

expected in other medical conditions [6], suggesting that CFS patients are sceptical of psychological interventions. Since the communication of the aim of a treatment is an intervention that can facilitate change [7], the controversy about the nature of improvement is clinically important.

To find out the tenable goal of therapy – adaptation or recovery – a definition of recovery is needed that can be operationalized and measured. We propose that a definition is used that closely follows the Center for Disease Control (CDC) criteria for CFS [8]. Two key elements of the CDC criteria are that a patient is severely fatigued and disabled. Recovery then implies that the patient's level of fatigue is within the range of healthy controls. We propose operationalizing this criterion as scoring *within the range of the mean plus (or minus) 1 standard deviation (SD)* of the healthy population.

A second aspect of recovery is that a patient will no longer be disabled. This means that patients have no physical disabilities – an often used criterion in CFS – and no disabilities in any other domains of functioning. Again, we propose scoring within the range of the mean plus 1 SD of the healthy population as the criterion for recovery. Although patients who are no longer abnormally fatigued *or* disabled do not meet the CDC criteria for CFS, having a 'normal' level of fatigue *and* not being disabled is a more satisfactory definition of recovery.

For complete recovery the perception of the patient also has to change. The patient has to perceive his fatigue and functioning as both normal and comparable to healthy people. Finally, a comprehensive definition combines changes in fatigue, disability and perception.

The objective of this study was to find out whether recovery is possible after CBT. For this, we collected data from a cohort of patients treated with CBT. For comparison we used healthy population norms. By doing this, we assumed that CFS was the only health problem of the patients. However, it is possible that the patient had another medical condition beside CFS, causing disability. Therefore, we measured the confounding effect of co-morbid medical conditions on the outcome.

Methods

Subjects

All consecutive patients with CFS that were treated with CBT at the Radboud University Nijmegen Medical Centre between September 2003 and May 2005 were eligible for the study if they met the following inclusion criteria:

1 CDC criteria for CFS [8];
2 severely fatigued and functionally impaired, defined by a cut-off score of 35 or higher on the fatigue severity subscale of the Checklist Individual Strength (CIS-fatigue) [9] and a weighted score of 700 or higher on the Sickness Impact Profile (SIP) [10];
3 completed the pre- and post-treatment assessment.

If a medical co-morbidity was present which could not explain the fatigue, it was registered for further analyses.

Intervention

All patients received CBT for CFS according to a protocol described elsewhere [11].

Assessment

The assessment was part of the clinical routine and performed by research assistants not involved in the treatment.

Self-Reported Improvement

Self-rated improvement was measured after treatment by one question: patients indicated whether they had no symptoms, significantly fewer symptoms, the same complaints or whether the symptoms had become worse [12].

Fatigue

The different definitions of recovery are summarized in table 1. The CIS-fatigue indicates the level of experienced fatigue over the past 2-week period and consists of 8 items on a 7-point scale. The score can range between 8 and 56 [9]. A normal group of 53 healthy adults with a mean age of 37.1 (SD 11.5) has a mean score on the CIS-fatigue of 17.3 (SD 10.1). Using this as a reference for the CBT group, there resulted a threshold score of 27, the mean plus 1 SD [13].

Disabilities

Physical disabilities were measured with the 'physical functioning' subscale of the Medical Outcomes Survey Short Form-36 (SF-36) [14, 15]. The scores range from 0 (maximum physical limitations) to 100 (ability to do vigorous activity). Healthy adults without a chronic condition [16] were used as a norm group, with a mean score of 93.1 (SD 11.7). A patient had to score 80 or higher to be considered as recovered.

Social functioning was measured with the subscale 'social functioning' of the SF-36, ranging between 0 (no social activities) and 100 (normal participation in social activities). Using the same criterion and reference group as above resulted in a threshold score for recovery of 75 or higher.

The SIP measures functional disability in ambulation, home management, mobility, alertness behaviour, sleep/rest, work limitations, social interactions, recreation and pastimes. The eight subscales were added to provide one weighted score of disability (SIP8 total). The mean SIP8 total score of a healthy group of 78 women is 65.5 (SD 137.8) [17]. Recovery was defined as scoring the same or lower than the mean plus 1 SD of this reference group, i.e. scoring 203 or lower.

Combining Fatigue and Disabilities

This definition of recovery was operationalized by combining cut-off scores on SF-36 physical functioning and the CIS-fatigue.

Table 1. Operationalization of the different definitions of recovery

Definition of recovery	Measure	Criterion used	Cut-off
Level of fatigue comparable to healthy people	CIS-fatigue	Mean + 1 SD	≤27
No physical disability	SF-36 physical	Mean – 1 SD	≥80
No social disability	SF-36 social	Mean – 1 SD	≥75
No disabilities in all domains	SIP8 total	Mean + 1 SD	≤203
Normal fatigue *and* no physical disability	CIS-fatigue, SF-36 physical	Mean + 1 SD, mean – 1 SD	≤27, ≥80
Normal health perception	SF-36 general health	Mean – 1 SD	≥65
No negative perception of fatigue	FQL	Factor score negative = 0	
Combining criteria of			
Fatigue	CIS-fatigue	Mean + 1 SD	≤27
Physical and social disabilities	SF-36 physical and social	Mean – 1 SD	≥80, ≥75
Perception of health	SF-36 general health	Mean – 1 SD	≥65
Perception of fatigue	FQL	Factor score negative = 0	

Mean = Mean of healthy norm group.

Table 2. Pre- and post-treatment scores of CIS-fatigue, SF-36 physical and SIP8 total (n = 96)

	Pre-treatment mean	Post-treatment mean	Treatment effect	95% CI	t value	d.f.	p value
Self-rated improvement, %		77					
CIS-fatigue	50.0 ± 5.2	30.3 ± 14.0	–19.7	–16.8 to –22.6	–13.6	95	<0.001
SF-36 physical	51.8 ± 19.1	76.3 ± 23.0	24.5	19.1 to 29.8	9.1	94	<0.001
SIP8 total	1,448 ± 510	682 ± 619	–766	–631 to –900	–11.3	95	<0.001

t values assessed by pairwise t test.

Perception of Health and Fatigue

Health perception was assessed with the scale 'general health perception' of the SF-36. This scale measures the evaluation of the health status by a patient, with scores ranging between 0 and 100. The mean in the reference group was 80 (SD 14.5) resulting in a cut-off score of 65.

The perception of fatigue was assessed with the Fatigue Quality List (FQL). The FQL consists of 18 adjectives and patients pick which adjectives best fit their experience of fatigue. Factor analysis showed a 4-factor solution; 3 of the 4 factors have negative connotations of fatigue: 'frustrating', 'exhausting' and 'frightening'. About 97% of the untreated CFS patients scored on 1 or more of the 3 factors [Gielissen et al., unpubl. data]. Recovery was defined as no longer scoring on any of the 3 negative factors.

Combining Fatigue, Disabilities and Perception

This comprehensive definition of recovery was operationalized by combining the cut-off scores on the CIS-fatigue, the SF-36 scales of physical functioning and social disabilities, the general health perception and the FQL.

Results

Baseline Data

Of the 112 CFS patients with a pre-treatment assessment, 3 (3%) did not start with CBT. There were 13 dropouts (11% of the patients starting with therapy) during treatment, so 96 patients completed the pre- and post-treatment assessment. The mean age of this group was 37.0 years (SD 11.5). Seventy-three patients were women (76%). The mean duration of the illness was 70.8 months (range 12–276 months, SD 52.8).

Treatment Results

Table 2 shows the scores of the patients before and after treatment. Following treatment, 73 (77%) of the 95 patients, who rated their improvement (data were missing for 1 patient), reported that they had no or significantly fewer symptoms. There was a significant decrease

in CIS-fatigue and patients also reported significantly fewer disabilities on the SF-36 subscale physical functioning and the SIP8. In total, 66 patients (69%) no longer met the inclusion criteria for fatigue severity and the level of disabilities (SIP8 ≥700).

Full Recovery as Outcome

The percentage of recovered patients was determined for all criteria and ranged between 23 and 59% (table 3).

The Effect of Medical Co-Morbidity

Twenty-two of the 96 patients (23%) had a medical co-morbid condition beside CFS. Fifteen patients had one medical co-morbidity: treated hyperthyroidism, gonadal dysgenesis with normal karyotype, menorrhagia, controlled diabetes mellitus, quiescent ulcerative colitis, nephrotic syndrome, controlled asthma, allergy (2), recurrent sinusitis, epilepsy, migraine, periodic leg movement disorder, multiple traumas, intramedullary haemangioma on medication. Seven patients had two co-morbidities: treated hyperthyroidism and epilepsy, controlled diabetes mellitus and Forestier's disease, controlled asthma and chronic low back pain (2), allergy and treated sleep apnoea, single transient ischaemic attack and cervical arthrosis, chronic headache and treated high blood pressure. After CBT, patients with medical co-morbidity had a mean CIS-fatigue score of 35.8 (SD 13.7) compared to a mean CIS-fatigue score of 28.6 (SD 14.0) for the group without ($t = 2.15$, d.f. 94, $p = 0.034$). The group with medical co-morbidity also had more SIP disabilities following CBT, compared to the group without co-morbidity ($t = 2.22$, d.f. 94, $p = 0.029$). The SIP8 total mean scores were 934 (SD 563) and 607 (SD 739), respectively. The SF-36 physical functioning following treatment was lower in the group with co-morbidity [mean of 66 (SD 27.9) and 80 (SD 20.4), respectively; $t = 2.46$, d.f. 94, $p = 0.016$]. Fewer patients with medical co-morbidity recovered (table 4). For social disability, the perception of fatigue, and the combination of all criteria for recovery, the difference in the proportions of recovered patients failed to reach statistical significance.

Discussion

More than 70% of the CFS patients reported significantly fewer symptoms following treatment with CBT and roughly 70% no longer met the CDC criteria for CFS.

Table 3. Percentage of patients (n = 96) who meet the definitions of recovery following CBT

Definition of recovery	Criterion reached, %
Level of fatigue comparable to healthy people	48
No physical disability	59
No social disability	55
No disabilities in all domains	26
Normal level of fatigue *and* no physical disability	44
Normal health perception	54
No negative perception of fatigue	37
Combining criteria of fatigue, disabilities and perception of health and fatigue	23

Table 4. Percentage of recovered patients following CBT with (n = 22) and without (n = 74) medical co-morbidity

Definition of recovery	No co-morbidity %	Co-morbidity %	Z value	p value
Level of fatigue comparable to healthy people	55	23	–2.68	0.007
No physical disability	65	41	–2.00	0.046
No social disability	59	50	–0.56	0.578
No disabilities in all domains	31	9	–2.05	0.040
Normal level of fatigue *and* no physical disability	50	23	–2.25	0.024
Normal health perception	58	41	–1.41	0.157
No negative perception of fatigue	41	23	–1.52	0.129
Combining criteria of fatigue, disabilities and perception of health and fatigue	29	12	–1.17	0.241

Z values determined by the Mann-Whitney U test.

This favourable outcome is consistent with the results of earlier controlled studies [1, 2].

Improvement and not meeting research criteria for an illness are different from recovering [18, 19]. To examine if recovery was possible we used different definitions of recovery that encompassed three elements: no longer being severely fatigued, being able to resume all activities, and a perception of health and fatigue that is similar to the perception of healthy persons. Depending on the definition used, up to 59% of the patients recovered. Even if we used the most conservative definition of recovery, 23% fully recovered. We therefore conclude that recovery from CFS following CBT is possible.

In the absence of a control treatment group, it is difficult to attribute this effect to treatment with certainty. A comparison with the natural course of CFS provides some useful information. In a review [20] that used less stringent criteria for recovery, the median recovery rate without treatment was 5% of the patients meeting operational criteria for CFS. As expected, the recovery rates following CBT found in this study were substantially higher. Our study was only concerned with the short-term effects of treatment. The only controlled study investigating the long-term efficacy of CBT for CFS showed lasting benefits 5 years after treatment [21].

Some may argue that it is not possible to recover from CFS and that our recovered patients were misdiagnosed. We found no evidence to support this, with all patients meeting CDC criteria for CFS. Ninety-one of our 96 patients complained of post-exertional malaise, which some suggest is the main characteristic feature of CFS [22].

The criteria for recovery were based on healthy norms. Patients had to score within the range of the mean plus or minus 1 SD. The norm groups were selected for their good health. Assuming a normal distribution, this means that 15% of the healthy subjects (scoring between 1 and 2 SD beyond the mean) had a score that would be considered as deviant from the norm in the present study. One could say that a patient meeting these criteria not only recovered from CFS, but is also more healthy than a substantial part of the healthy general public. Thus, the effect of CBT may be underestimated.

In determining the threshold scores for recovery we assumed a normal distribution of scores. However, in the healthy population the SIP and SF-36 scores were not normally distributed. Therefore one could argue that recovery according to the SIP8 has to be defined as scoring the same or lower than the 85th percentile of the healthy reference group. In that case, the recovery rate using the definition of having no disabilities in all domains (i.e. scoring the same or lower than the 85th percentile on the SIP8) would decrease from 26 to 20%. As we do not know the exact distribution of the SF-36 scores, we cannot control for the effects of violation of the assumption of normality.

Patients with medical co-morbidities had significantly higher levels of disabilities after treatment. This implies that less stringent criteria for recovery should be used that incorporate the effect of the co-morbidity. Using healthy adults as a reference group will lead to an underestimation of the effect of CBT in those with medical co-morbid conditions.

The fact that fatigue, disability and health can return to a 'normal' level following treatment is a promising finding. Keeping in mind that most patients suffered several years of ill health, it is remarkable that such a change in perception can take place. These results suggest that recovery after CBT may be possible when it is applied to other related disorders for which CBT has been found to be helpful, such as fibromyalgia [23].

The first clinical implication of the present study is that a therapist delivering CBT can tell the patient that substantial improvement is likely to occur and that full recovery is possible. By communicating this, the therapist can counterbalance factors that lower the expectations of the patient. Examples of such factors are a negative attitude of certain patient advocacy groups towards behavioural interventions or an oversolicitous attitude of significant others in response to CFS [24]. There is empirical evidence that lower expectations of patients have a negative influence on therapy outcome [25].

The second clinical implication of the present study is that recovery is a construction. The percentage of recovered patients differed depending on the definition of recovery used. It is possible that a patient has another concept of recovery than the therapist. It is important that they jointly (re)formulate a definition which forms the objective of the treatment.

References

1 Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD, Ramirez G: Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. J Am Med Assoc 2001;286:1360–1368.
2 Stulemeijer M, de Jong LWAM, Fiselier TJW, Hoogveld SWB, Bleijenberg G: Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial. Br Med J 2005;330:7481–7486.
3 Prins JB, Bleijenberg G, de Boo TM, van der Meer JWM: Cognitive behaviour therapy for chronic fatigue syndrome: correspondence, authors reply. Lancet 2001;358:240–241.
4 Fava GA: The concept of recovery in affective disorders. Psychother Psychosom 1996; 65:2–13.
5 Andrews G: Should depression be managed as a chronic disease? Br Med J 2001;322:419–421.
6 Cho HJ, Hotopf M, Wessely S: The placebo response in the treatment of chronic fatigue syndrome: a systematic review and meta-analysis. Psychosom Med 2005;67:301–313.
7 Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijne J: Influence of context effects on health outcomes: a systematic review. Lancet 2001;357:757–762.
8 Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A: The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. Ann Intern Med 1994;121:953–959.
9 Vercoulen JHMM, Swanink CMA, Fennis JFM, Galama, JMD, van der Meer JWM, Bleijenberg G: Dimensional assessment of chronic fatigue syndrome. J Psychosom Res 1994;38:383–392.
10 Van der Werf SP, De Vree B, van der Meer JWM, Bleijenberg G: Natural course and predicting self-reported improvement in patients with a relatively short illness duration. J Psychosom Res 2003;53:749–753.
11 Bleijenberg G, Prins J, Bazelmans E: Cognitive behavioral therapies; in Jason LA, Fennell PA, Taylor RR (eds): Handbook of Chronic Fatigue Syndrome. New York, Wiley & Sons, 2003, pp 493–526.
12 Prins JB, Bleijenberg G, Bazelmans E, Elving L, de Boo TM, Severens JL, van der Wilt GJ, Spinhoven P, van der Meer JWM: Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. Lancet 2001;357:841–847.
13 Vercoulen JHMM, Alberts M, Bleijenberg G: De Checklist Individual Strength (CIS) (The Checklist Individual Strength). Gedragstherapie (Behavioural Therapy) 1999;32: 642–649.
14 Stewart A, Hays R, Ware J: The MOS short form general health survey: reliability and validity in a patient population. Med Care 1988;26:724–732.
15 Ware JE Jr, Sherbourne CD: The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–483.
16 Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R, Sprangers MA, te Velde A, Verrips E: Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease population. J Clin Epidemiol 1998;51:1055–1068.
17 Servaes P, Verhagen C, Bleijenberg G: Determinants of chronic fatigue in disease-free breast cancer patients, a cross-sectional study. Ann Oncol 2002;13:589–598.
18 Pasquali R: The biological balance between psychological well-being and distress: a clinician's point of view. Psychother Psychosom 2006;75:69–71.
19 Ryff CD, Dienberg Love G, Urry HL, Muller D, Rosenkranz MA, Friedman EM, Davidson RJ, Singer B: Psychological well-being and ill-being: do they have distinct or mirrored biological correlates? Psychother Psychosom 2006;75:85–95.
20 Cairns R, Hotoph M: A systematic review describing the prognosis of chronic fatigue syndrome. Occup Med C 2005;55:20–31.
21 Deale A, Husain K, Chalder T, Wessely S: Long-term outcome of cognitive behaviour therapy versus relaxation therapy for chronic fatigue syndrome: a 5-year follow-up study. Am J Psychiatry 2001;158:2038–2042.
22 White PD, Thomas JM, Amess J, Grover SA, Kangro HO, Clare AW: The existence of a fatigue syndrome after glandular fever. Psychol Med 1995;25:907–916.
23 van Houdenhove B, Egle UT: Fibromyalgia: a stress disorder? Psychother Psychosom 2004;73:267–275.
24 Prins JB, Bos E, Huibers MJ, Servaes P, van der Werf SP, van der Meer JW, Bleijenberg G: Social support and the persistence of complaints in chronic fatigue syndrome. Psychother Psychosom 2004;73:174–182.
25 Bentall RP, Powell P, Nye FJ, Edwards RH: Predictors of response to treatment for chronic fatigue syndrome. Br J Psychiatry 2002;181:248–252.