The effect of cognitive behaviour therapy for chronic fatigue syndrome on self-reported cognitive impairments and neuropsychological test performance

Hans Knoop, Judith B Prins, Maja Stulemeijer, Jos W M van der Meer and Gijs Bleijenberg

J. Neurol. Neurosurg. Psychiatry 2007;78;434-436
doi:10.1136/jnnp.2006.100974

SHORT REPORT

The effect of cognitive behaviour therapy for chronic fatigue syndrome on self-reported cognitive impairments and neuropsychological test performance

Hans Knoop, Judith B Prins, Maja Stulemeijer, Jos W M van der Meer, Gijs Bleijenberg

J Neurol Neurosurg Psychiatry 2007;**78**:434–436. doi: 10.1136/jnnp.2006.100974

Background: Patients with chronic fatigue syndrome (CFS) often have concentration and memory problems. Neuropsychological test performance is impaired in at least a subgroup of patients with CFS. Cognitive behavioural therapy (CBT) for CFS leads to a reduction in fatigue and disabilities.
Aim: To test the hypothesis that CBT results in a reduction of self-reported cognitive impairment and in an improved neuropsychological test performance.
Methods: Data of two previous randomised controlled trials were used. One study compared CBT for adult patients with CFS, with two control conditions. The second study compared CBT for adolescent patients with a waiting list condition. Self-reported cognitive impairment was assessed with questionnaires. Information speed was measured with simple and choice reaction time tasks. Adults also completed the symbol digit-modalities task, a measure of complex attentional function.
Results: In both studies, the level of self-reported cognitive impairment decreased significantly more after CBT than in the control conditions. Neuropsychological test performance did not improve.
Conclusions: CBT leads to a reduction in self-reported cognitive impairment, but not to improved neuropsychological test performance. The findings of this study support the idea that the distorted perception of cognitive processes is more central to CFS than actual cognitive performance.

Chronic fatigue syndrome (CFS) is characterised by severe fatigue, lasting longer than 6 months and leading to functional impairment. The fatigue is not the result of a known organic disease or ongoing exertion, and not alleviated by rest. According to the Centre for Disease Control definition of CFS, impaired concentration and/or memory is an additional symptom criterion.[1] The level of self-reported cognitive impairments in CFS is high[2] and contributes to the social and occupational dysfunctions of patients with CFS.[3]

Studies evaluating neuropsychological functioning in patients with CFS with neuropsychological tests yielded conflicting results.[4] Reduced speed of (complex) information processing is the most consistently found impairment.[3 5 6] However, several studies found no cognitive impairments[7] and other studies identified a subset of patients with defective performance.[8 9]

Fatigue-related cognitions and behaviour can perpetuate CFS.[10] Several controlled trials have shown that cognitive behavioural therapy (CBT) aimed at these perpetuating factors leads to a reduction in fatigue and disabilities.[11]

The first hypothesis tested was that CBT for CFS also results in a reduction of self-reported cognitive impairments. The second hypothesis was that the neuropsychological test performance of patients with CFS improves after CBT. Data of two previous CBT trials[12 13] were used to test the hypotheses.

MATERIALS AND METHODS

Patients

The first study from which data were used compared the effects of CBT for adults with CFS with natural course and support groups[12] in a multicentre randomised controlled trial. Assessments were done at baseline, and at 8 and 14 months. An intention-to-treat analysis showed a reduction in fatigue and functional impairment after CBT. In two of the three participating treatment centres, neuropsychological tests were part of the assessments. Consequently, data from neuropsychological test performance were available for a subset of 233 (78 CBT; 76 natural course; 79 support group) of the total group of 278 patients. The mean (SD) age of this group was 36.8 (10.2) years, 182 (78%) were female and median illness duration was 41 months. The second study was a randomised controlled trial comparing CBT for adolescents with CFS[13] with a waiting list condition. A total of 69 patients were randomly assigned to the conditions. Assessments were done at baseline and at 5 months. The results showed a greater decrease in fatigue and functional impairment in the CBT group. Neuropsychological data of 67 patients were available (33 CBT; 34 waiting list). The mean (SD) age of the group was 15.6 (1.3) years, 59 (88%) were female and median illness duration was 18 months.

Questionnaires assessing self-reported cognitive impairments

Checklist individual strength-concentration

In both studies, the severity of concentration problems over the past 2 weeks was assessed with the subscale concentration of the checklist individual strength (CIS) that consists of five items on a seven-point scale. The score can range between 5 and 35.[3 12 13]

Sickness impact profile-alertness behaviour

In adults, the self-observed effect of cognitive impairments on daily functioning was assessed with the subscale sickness impact profile-alertness behaviour (SIP-ab) of the sickness impact profile.[14] The subscale has 10 items, each item is weighed and the score can range between 0 and 777. No such instrument was available for adolescents.

Abbreviations: CBT, cognitive behavioural therapy; CFS, chronic fatigue syndrome; CIS, checklist individual strength; CIS-conc, checklist individual strength-concentration; SDMT, symbol digit modalities task; SIP-ab, sickness impact profile-alertness behaviour; SOCI, self-observation of cognitive impairment

Table 1 Estimated treatment effect in change score (95% CI) on the dependent variables

Self-reported cognitive impairments			
Adults	CBT	Natural course	Support group
CIS-conc	−7.4 (−9.1 to −5.7)†	−2.7 (−4.4 to −1.0)**	−3.4 (−5.1 to −1.8)**
SIP-ab	−116 (−156 to −76)‡	−31 (−72 to −10)**	−61 (−100 to −21)
Adolescents	CBT	Waiting list	
CIS-conc	−6.8 (−10.5 to −3.5)‡	−0.9 (−4.2 to +2.5)*	
SOCI	−7.9 (−12.8 to −2.9)§	0.9 (−4.1 to +6.0)*	
Neuropsychological test performance			
Adults	CBT	Natural course	Support group
Simple reaction time (ms)	9 (−9 to 27)	−5 (−23 to 14)	6 (−12 to 24)
Choice reaction time (ms)	−24 (−51 to 3)	−27 (−54 to 1)	−26 (−53 to 1)
SDMT	2.8 (0.8 to 4.8)	2.3 (0.2 to 4.4)	4 (2 to 6)
Adolescents	CBT	Waiting list	
Simple reaction time (ms)	−30 (−53 to −8)	−18 (−41 to 4)	
Choice reaction time (ms)	−12 (−29 to 6)	−10 (−28 to 8)	

CBT, cognitive behavioural therapy; CIS-conc, checklist individual strength-concentration; SDMT, symbol digit modalities task; SIP-ab, sickness impact profile-alertness behaviour; SOCI, self-observation of cognitive impairment.
* Significantly different from the CBT condition, $p<0.05$.
**Significantly different from the CBT condition, $p<0.01$.
†Cohen's d based on change within treatment condition = 1.3.
‡Cohen's d = 0.6.
§Cohen's d = 0.4.

Self-observation of cognitive impairment

In adolescents, the frequency of cognitive impairments was determined with a structured diary. Patients rated both concentration and memory impairment separately on a daily self-observation list four times a day for 12 days (0 = no impairment; 1 = impaired). The percentage of concentration problems and memory problems (both number of assessments with a problem divided by 48 times 100) were added and then divided by two to calculate the mean percentage of incidents of cognitive impairment.

Neuropsychological tests

Reaction time task

The reaction time task consisted of two subtests, simple and choice reaction time tasks. Both are described in detail elsewhere.[8 15] In a previous study, the reaction times of patients with CFS were slower than that of healthy controls on both tasks.[8]

Symbol digit modalities task

The symbol digit modalities task (SDMT)[16] was used in the adult study as a measure of complex attention. In previous studies, patients with CFS scored lower than a matched healthy control group.[8 9]

Statistical analysis

Statistical analysis was performed using SPSS V.12.01. Significance was assumed at $p<0.05$. A multivariate analysis of variance was performed with self-reported cognitive impairment and reaction time as dependent variables and treatment as fixed factor. Univariate tests and post hoc analysis are reported if the multivariate test was significant. For the SDMT, a univariate analysis was performed, as data were available for a subset of 174 patients as the SDMT was added later to the test battery. In the adult study, the dependent variables were the change scores at 14 months from baseline and in the adolescent study, it was at 5 months from baseline. Reaction times were transformed by a logarithm transformation. For adults, if data at 14 months were missing and data 8-months post-treatment were available, the second were used. In all other cases, missing data were replaced with estimates derived by single imputation (missing variable analysis regression in SPSS with baseline value as predictor). For significant treatment effects, effect sizes were calculated.

RESULTS

Nineteen adult patients (8%) had missing checklist individual strength-concentration (CIS-conc) and SIP-ab post-treatment data. One patient had missing data on both reaction time tasks at baseline, for 44 (19%) patients only baseline data and for 30 (17%) patients only a baseline SDMT score was available.

Two adolescent patients had no SOCI scores at baseline. For 4 (6%) patients the CIS-conc and SOCI at second assessment were missing. Two patients had no baseline reaction time and for 13 (20%) adolescents the reaction times at the second assessment were missing.

In both studies, there were more data missing from neuropsychological tests than from questionnaires as some patients were willing to mail the questionnaires, but refused to undergo a second neuropsychological assessment.

Self-reported cognitive impairments

Adults

The multivariate test (Pillai's trace) showed a significant change in self-reported cognitive impairments ($F_{(4,460)} = 4.76$; $p = 0.001$). The univariate tests showed a significant effect of treatment on the change in CIS-conc and SIP-ab ($F_{(2,230)} = 8.94$; $p < 0.001$ and $F_{(2,230)} = 4.42$; $p = 0.013$). Following CBT, the decrease in CIS was significantly greater than in both the natural course ($p<0.001$) and the support group ($p = 0.001$; table 1). There was a significantly greater decrease in SIP-ab score after CBT compared with natural course ($p = 0.004$). The difference between CBT and support group failed to reach significance ($p = 0.055$).

Adolescents

The multivariate test showed a significant treatment effect on self-reported cognitive impairments ($F_{2,62} = 5.03$; $p = 0.009$). Univariate tests showed that the decrease in the CIS-conc and SOCI score was significantly larger in the CBT group ($F_{(1,63)} = 6.4$; $p = 0.014$ and $F_{(1,63)} = 6.28$; $p = 0.015$).

Neuropsychological test performance

Adults

There was no significant effect of treatment on either reaction time task ($F_{(4, 458)} = 0.44$; $p = 0.783$). There was no significant treatment effect on the SDMT ($F_{(2,171)} = 0.73$; $p = 0.484$).

Adolescents

Multivariate tests showed no significant treatment effect on either reaction time task ($F_{(2,62)} = 0.34$; $p = 0.714$).

DISCUSSION

The hypothesis that self-reported cognitive impairments decrease after CBT in patients with CFS was confirmed. Only one comparison in the adult study, measuring cognitive impairments more indirectly, showed an effect in the expected direction without reaching significance. The results of the original adolescent study[13] already indicated that concentration problems decrease after CBT. In that study, the concentration problems were assessed with a single item evaluating these problems retrospectively over a period of 6 months. This assessment can be easily influenced by situational circumstances and memory biases, which can be prevented by the use of a diary as in the present study. No support could be found for the hypothesis that neuropsychological test performance improves after CBT.

A methodological problem is that in a substantial part of the patients the neuropsychological data of the second assessment were missing. Furthermore, in our analysis we assumed that dropout occurred at random, whereas patients may drop out for non-random reasons. We repeated the analyses, but only on patients who completed both assessments. Again, there was no significant treatment effect. Our interpretation is that this indicates that improvement in self-reported cognitive impairments after CBT is independent of the change in neuropsychological test performance.

A discrepancy between subjectively reported disabilities versus objectively measured performance is not limited to the current study. Mahurin *et al*[17] found that the objective cognitive functioning of monozygotic twins discordant for CFS did not differ, whereas the twin with CFS reported more cognitive impairments. Metzger and Denney[18] showed that patients with CFS underestimated their cognitive performance. In the study by Vercoulen *et al*,[8] most patients with CFS reported concentration and memory problems, whereas only a small percentage showed an impaired performance. Given the fact that patients with CFS perceive their cognitive processes as impaired but underestimate their actual performance, one would expect that an effective treatment of CFS would lead to a more accurate perception of one's performance. The results of the present study are consistent with this prediction. CBT resulted in decreased complaints about cognitive functioning, but not in a change in performance. This is also in line with the hypothesis that a distorted perception of symptoms and performance is a crucial element of CFS.[10]

ACKNOWLEDGEMENTS

The authors thank Theo Fiselier for contributing to the selection of adolescent patients with CFS, Lammy Elving for contributing to the selection of adult patients and Ria te Winkel and Lida Nabuurs for assisting in data collection.

Authors' affiliations

Hans Knoop, Gijs Bleijenberg, Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
Judith B Prins, Maja Stulemeijer, Department of Medical Psychology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
Jos W M van der Meer, Department of Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Funding: The Health Insurance Council (College van Zorgverzekeraars) funded the adult CBT study. The Children's Welfare Stamps Netherlands (Stichting Kinderpostzegels Nederland) and the ME Foundation (ME Stichting) funded the adolescent CBT study.

Competing interests: none.

Correspondence to: H Knoop, Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, P O Box 9011, 6525 EC Nijmegen, The Netherlands; j.knoop@nkcv.umcn.nl

Received 26 June 2006
Revised 14 November 2006
Accepted 15 November 2006

REFERENCES

1 **Fukuda K**, Straus SE, Hickie I, *et al*. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med* 1994;**121**:953–9.
2 **Vercoulen JHMM**, Swanink CMA, Fennis JFM, *et al*. Dimensional assessment of chronic fatigue syndrome. *J Psychosom Res* 1994;**38**:383–92.
3 **Michiel V**, Cluydts R. Neuropsychological functioning in chronic fatigue syndrome: a review. *Acta Psychiatr Scand* 2001;**103**:84–93.
4 **Cho, HJ, Skowera, A, Cleare A, et al**. Chronic fatigue syndrome: an update focusing in phenomenology and pathophysiology. *Curr Opin Psychiatry* 2006;**19**:67–73.
5 **Moss-Morris R**, Petrie KJ, Large RG, *et al*. Neuropsychological deficits in chronic fatigue syndrome: artefact or reality? *J Neurol Neurosurg Psychiatry* 1996;**60**:474–7.
6 **Tiersky LA**, Johnson SK, Lange G, *et al*. The neuropsychology of chronic fatigue syndrome: a critical review. *J Clin Exp Neuropsychol* 1997;**19**:560–86.
7 **Dipino RK**, Kane RL. Neurocognitive functioning in chronic fatigue syndrome. *Neuropsychol Rev* 1996;**6**:47–60.
8 **Vercoulen JH**, Bazelmans E, Swanink CM, *et al*. Evaluating neuropsychological impairment in chronic fatigue syndrome. *J Clin Exp Neuropsychol* 1998;**20**:144–56.
9 **Van der Werf S**, Prins JB, Jongen P, *et al*. Abnormal neuropsychological findings are not necessarily a sign of cerebral impairment: a matched comparison between chronic fatigue syndrome an multiple sclerosis. *Neurol Neuropsychol Behav Neurol* 2000;**13**:199–203.
10 **Prins JB**, Van der Meer JWM, Bleijenberg G. Chronic fatigue syndrome. *Lancet* 2006;**376**:346–55.
11 **Whiting P**, Bagnall AM, Sowden AJ, *et al*. Interventions for the treatment and management of chronic fatigue syndrome; a systematic review. *J Am Med Assoc* 2001;**286**:1360–8.
12 **Prins JB**, Bleijenberg G, Bazelmans E, *et al*. Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. *Lancet* 2001;**357**:841–7.
13 **Stulemeijer M**, de Jong LWAM, Fiselier TJW, *et al*. Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial. *BMJ* 2005;**330**:7481–6.
14 **Berger M**, Bobbit RA, Carter WB, *et al*. The sickness impact profile: development and final revision of a health status measure. *Med Care* 1981;**19**:787–805.
15 **Jolles J**. *Maastricht aging study: determinants of cognitive aging*. Maastricht: Neuropsychological Publishers, 1995.
16 **Stinnissen J**, Willems PJ, Coetsier L, *et al*. *Handleiding bij de Nederlandse bewerking van de WAIS [Manual of the Dutch edition of the WAIS]*. Amsterdam: Swets and Zeitlinger, 1970.
17 **Mahurin RK**, Claypoole KH, Goldberg JH, *et al*. Cognitive processing in monozygotic twins discordant for chronic fatigue syndrome. *Neuropsychology* 2004;**18**:232–9.
18 **Metzger FA**, Denney, DR. Perception of cognitive performance in patients with chronic fatigue syndrome. *Ann Behav Med* 2002;**24**:106–12.