Cognitive Behaviour Therapy in Patients with Chronic Fatigue Syndrome: the Role of Illness Acceptance and Neuroticism

Carine Poppe[1*], Mirko Petrovic[2], Dirk Vogelaers[1], Geert Crombez[3]

[1]Department of General Internal Medicine, Ghent University Hospital, Belgium

[2]Department of Geriatric Medicine, Ghent University Hospital, Belgium

[3]Department of Experimental-Clinical and Health Psychology, Ghent University, Belgium

***Corresponding Author**

Carine Poppe, MPsych, PhD

Department of General Internal Medicine, Ghent University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium.

Tel: +32 9 332.55.12, Fax: +32 9 332 64 89

Email: Carine.Poppe@ugent.be

Number of words: 4560

Number of tables: 3

Running head: CBT and chronic fatigue syndrome

Key Words: chronic fatigue syndrome, cognitive behaviour therapy, acceptance, health-related quality of life, neuroticism.

Abstract

Objective. Increasing the quality of life (QoL) of patients with chronic fatigue is challenging because recovery is seldom achieved. Therefore, it is important to identify processes that improve QoL. This study examined the extent of improvement related to cognitive behaviour group therapy (CBT), and whether improvement is affected by initial levels of acceptance and neuroticism.

Methods. Eighty CFS patients followed CBT, and self-reported (pre-post design) on mental and physical QoL (MQoL and PQoL), fatigue, acceptance, neuroticism. The extent of improvement was analyzed using t-tests, effect sizes, and clinically significant change criteria. Whether acceptance and neuroticism at baseline predicted changes, was analyzed by means of correlation and regression analyses.

Results. Significant improvement was found for all variables. The effect size for MQoL and PQoL was small; for acceptance and fatigue moderate. About 20% (MQoL) to 40% (fatigue) of the participants clinically improved.

Pre-treatment level of acceptance was negatively correlated with changes in MQoL, not with PQoL changes. Neuroticism pre-treatment was positively related with MQoL changes. Regression analysis showed an effect of acceptance on changes in MQoL beyond the effect of neuroticism.

Conclusions: Although CBT is an evidence-based treatment, the sizes of the effects are often small regarding QoL. Our study also revealed small effect sizes. Our study showed that patient characteristics at baseline were significantly associated with MQoL outcome; indicating that CFS patients with high neuroticism or with a low acceptance show more improvement in MQoL. We propose to specifically target acceptance and neuroticism before treatment in order to maximize clinical relevance.

Introduction

Chronic fatigue syndrome (CFS) is a complex syndrome with severe disabling fatigue lasting for at least 6 months as the major criterion according to Centre for Disease Control [1]. The precise medical pathophysiology remains unknown, and many researchers adopt a bio-psycho-social account for this 'medically unexplained syndrome', acknowledging the importance of complex and dynamic interactions between biological, psychological and social factors. Within this account, cognitive behavioural models have become increasingly popular [2-5]. These models propose a set of predisposing factors (e.g., genetics, personality characteristics, and life events), precipitating factors (e.g., physiological factors and general distress) and perpetuating factors (e.g., physiological, cognitive, behavioural, and social reactions) that each may contribute to the development and maintenance of CFS [3-8].

Cognitive behavioural models are equally well used to deliver treatments for CFS. Most often cognitive-behavioural therapy (CBT) for CFS targets cognitive and behavioural perpetuating factors such as the misbalance between rest and activity, and the belief that they have to be perfect in every situation, potentially resulting in ignoring their physical limits. Research has shown that CBT improves physical functioning and fatigue reduction immediately and some time after treatment [9,10]. Nevertheless, complete recovery is uncommon.

A recent meta-analytical study of Castell and colleagues shows an overall effect size for CBT of 0.33, which is small according to Cohen's recommendations [10,11]. This research group suggested that the variability in fatigue outcomes in CBT reflects the existence of moderating variables and examined illness characteristics and treatment characteristics. Regarding *illness characteristics*, illness duration does not affect the outcome of CBT in CFS. Regarding *treatment characteristics*, total duration of CBT (in hours) showed a positive influence on the outcome. No evidence was found that the treatment format (group or individual) and treatment duration (weeks) affected the effect size of CBT [10]. Although group programs are often preferred because of the cost efficacy and they involve peer support, support groups without therapy do not yield similar outcome results as CBT [12].

Other studies indicate that *patient characteristics also* matter: CBT effect increases when patients are less focused on their symptoms and are less anxious about it [13-14]. Until now the role of illness acceptance in CBT has received little attention [15].

Illness acceptance is defined as "recognizing the need to adapt to a chronic illness while perceiving the ability to tolerate the unpredictable, uncontrollable nature of the disease, and handle its adverse consequences" [16-p1027]. This way of coping with adversity is more

and more acknowledged to be related to a good adjustment to chronic illness [17-22]. Its function is also well-articulated in self-regulatory models of coping [23-25].One example of such a model is the 'Dual-Process Model of Coping of Brandtstädter and colleagues' [26-27], which distinguishes between two complementary coping strategies: accommodative coping and assimilative coping. 'Assimilative coping' is characterized by active attempts to control the stressor and solve the problem, in order to continue with the pursuit of one's life goals. When a problem remains insoluble and blocks life goals, stress increases and a transition from assimilative to accommodative coping may be required. In accommodative coping "the structure of individual cognitions and valuations is modified to make the given situation appear less negative or more acceptable" that leads to the disengagement from the blocked goals, and goal adjustment or reengagement with feasible goals [26-p58]. Acceptance of the adverse consequences and uncontrollability of an insoluble problem is often considered as a key process in accommodative coping [16, 28]. Chronic illness, such as CFS, may be considered as a problem that cannot (yet) be cured or solved, and where an accommodative coping strategy and illness acceptance is to be preferred. In line with this view, cross-sectional studies indicate that acceptance plays a role in adjustment to chronic illnesses, amongst which CFS and that acceptance has been found to be associated with a better mental health-related quality of life (MQoL) [17, 27, 29-31]. Of further interest are the results of Brooks and colleagues, who found that CBT for CFS resulted in an increase of acceptance, and that lack of acceptance was associated with fatigue and physical functioning [15]. In our study, we are interested whether acceptance before the start of CBT predicts the effects of treatment regarding health-related quality of life and fatigue.

Another patient characteristic which we will examine in relation to CBT treatment is the personality. Personality traits are related to how individuals cope with problems [32]. In particular the trait 'neuroticism', which is characterized as the degree of emotional instability, associated with a tendency to experience negative emotions, a vulnerability for stress and for psychopathology, may be relevant [33]. First, neuroticism is presumed to be one of the predisposing factors of CFS in [4-5,34] in biopsychosocial accounts. Second, there is preliminary evidence that neuroticism negatively influences illness acceptance and mental wellbeing in CFS [31]. In our study, therefore, we wanted to examine whether neuroticism before treatment negatively influences the effects of CBT.

Next to fatigue, quality of life (QoL) should be a substantial outcome parameter to evaluate the condition of patients after treatment. QoL often has two dimensions: a mental health quality of life (MQoL) and a physical health quality of life (PQoL). Increasing QoL in

patients with CFS is a challenge because recovery is difficult to achieve. Research shows that the QoL is lower in CFS patients compared with other chronic ill and healthy control groups [35-37]. One of the possible reasons is that overall patients with CFS score higher on neuroticism, which is related to a more negative perception of symptoms, disability, and health [38-39]. Another reason might be that patients with CFS have difficulties with accepting the fatigue and its devastating consequences, especially because CFS is regarded as a medically unexplained illness [8]. Although it has already been shown that non-accepting cognitions seem to lead to maladaptive activity patterns in patients with CFS which results in increased fatigue, frustration and a negative QoL [30-31, 40-41], more research is needed to highlight the importance of acceptance for adjusting to a life with CFS.

In sum, this study examined the extent of improvement related to cognitive behaviour group therapy (CBT) on MQoL and PQoL, fatigue and acceptance, using a pre-post design without no-treatment control group, and, of most importance to this study, whether the observed improvement in outcomes is affected by initial levels of acceptance and neuroticism. We will use three methods (statistical, practical, and clinical) to evaluate the pre-post treatment changes in mental, and physical health-related QoL, fatigue and acceptance.

Method

Participants

Patients with CFS from the general internal medicine outpatient clinic of the Ghent University Hospital were invited to participate in the study in the period 2009-2011. They experienced group CBT over a period of 6 months. The pre-treatment data were collected during a psychological assessment phase, which was a part of a multidisciplinary diagnostic procedure. In this procedure psychological assessment was the second examination after the diagnostic investigation by the internist. The psychological assessment was followed by a psychiatric assessment and a multidisciplinary patient discussion, in which the diagnosis of CFS according to the Fukuda et. al. criteria [1] is made and treatment modalities are discussed. Between the baseline measurement and the start of CBT-treatment there was a period of approximately 4-6 months. The post-treatment data were collected at the end of the treatment. The duration of the treatment was 6 months. There was a mean of 12.4 months between pre and post-treatment measurement. The number of group members ranged from 8-12. All patients provided informed consent, and the study was approved by the local ethics

committee. Inclusion criteria of the study were: knowledge of Dutch language (in order to fill-in the Dutch questionnaires), age (minimum 18 years old), and a diagnosis of CFS according to the CDC criteria [1] with a strict exclusion for medical (internal and psychiatric) diagnoses that could explain the fatigue symptoms. The data from the pre-treatment questionnaires of the patients who did not complete the treatment program were excluded, which resulted in 80 patients (73 women and 7 men). Various reasons were given for drop-out: impossible combination work-therapy, other medical diagnoses received during treatment, and family circumstances.

The group CBT was conducted by four psychologists trained by a cognitive behavioural therapist for this program. We chose a group CBT programme because of cost efficacy and the putative value of the peer support. CBT aimed at increasing functioning, and its objective and content are comparable with manuals of other CBT trials [9,12]. The treatment program consisted of twelve, 2-hour sessions, and a session was held every 2 weeks. The program included stress management (psycho-education on stress and fatigue and a relaxation therapy according to the Jacobson technique); gradual activity management (in the first phase patients are learning to find a balance between rest and activity by activity planning, in a second phase, activity was gradually built up); sleep management (psycho-education on sleep hygiene and sleep disorders, and stimulating a regular sleep pattern); and cognitive therapy (identifying and challenging negative cognitions about fatigue; and cognitive restructuring) [9]. No specific interventions regarding acceptance were included.

Measures

In this study we used self-report questionnaires to assess the following variables: mental and physical QoL, fatigue severity, acceptance, and neuroticism. All participants completed the questionnaires described below.

The 36-item Short Form Health Survey (SF-36)

The SF-36 is a 36-item questionnaire that consists of 8 subscales: 4 mental health subscales (vitality, social functioning, role-emotional, and mental health) and four physical health subscales (physical functioning, role-physical, bodily pain, and general health). There are two summary scores, the ‘mental and physical component summary scores’, which are used for our analyses. MQoL and PQoL refer to these summary scores. The items are scored on a 2- to 6-point Likert scale with the total scores transformed to scale values from 0 to 100.

The higher the summary scores, the better the quality of life. The SF-36 is a reliable and valid instrument with a Cronbach's alpha coefficient of 0.90 [42-43].

Checklist interpersonal attachment strength (CIS)

We used the '*fatigue severity'* subscale of the CIS as an indicator of fatigue. The CIS is a 20-item questionnaire with 4 subscales: 'Fatigue severity' (8 items; e.g., 'I feel tired'); 'Concentration' (5 items); 'Motivation' (4 items); and 'Physical activity level' (3 items). The items are scored on a 7-point scale (from '0=correct' to '6=incorrect'). The total scores are transformed to scores from 0-7. The CIS has been shown to have good reliability and validity, and the subscale 'fatigue severity', which we used in our study, has a Cronbach's alpha coefficient of 0.88 [44].

Illness Cognition Questionnaire (ICQ)

Acceptance was assessed by the subscale '*acceptance'* of the ICQ. The questionnaire has three subscales, each with 6 items: 'Acceptance' (e.g., 'I have learned to accept the disability of my disease'), 'Helplessness', and 'Disease benefits'. Items are scored on a 4-point scale with a range from 1 to 4 (from 1= disagree to 4= totally agree). The maximum score is 24. The ICQ is a reliable and valid instrument, with a Cronbach's alpha of 0.90 for the acceptance subscale [16, 28].

NEO-Five Factor Inventory (NEO-FFI)

This 60-item Dutch version of the revised NEO Five Factor Inventory measures 5 personality traits: neuroticism, extraversion, openness, agreeableness, and conscientiousness, based on the Big Five Personality model. Each trait consists of 12 items, and each item is scored on a 4-point scale (from '0=totally disagree' to '4=totally agree'). Only the trait *'neuroticism'* was used in our analyses. Research has shown that the NEO-FFI is sufficiently reliable (alpha coefficients vary between 0.68 and 0.86). Also the construct and concurrent validity has been well documented [45-46]. Neuroticism was measured only at pre-treatment as we considered this personality trait to be a stable characteristic.

Data analyses

Data were analysed with SPSS version 19.0.

First, we investigated the pre-post treatment changes ($X_{change} = X_{post} - X_{pre)}$ in MQoL, PQoL, fatigue and acceptance using statistical, practical, and clinical criteria [47-52]. Next, we investigated whether the changes after cognitive behaviour group therapy (CBT) in MQoL/PQoL and fatigue were affected by initial levels (before treatment) of acceptance and neuroticism scores. For all analyses, there were no problems with regard to normality or collinearity.

Analyses of pre-post CBT changes

We used paired sample t-test to test whether post-CBT scores were *statistically significant* from pre-CBT scores for MQoL, PQoL, fatigue and acceptance [50].

We used independent Cohen's d as effect size to identify the *practical significance* of the observed pre-post CBT changes. Cohen's d = (M1 – M2) / SD pooled. Cohen's d is a standardized difference score, and provides an index that allows easy comparison between different outcomes [48-50]. For comparison with the norms of Cohen (1988), we calculated effect sizes for independent samples using the formula of Dunlap and colleagues (see Borenstein et al., 2009) [53-54]. Means, standard deviation from both the pre- and post-measurement were used, as well as the correlation between the pre- and post measure [53].

Finally we explored the *clinical significance* of the pre-post CBT change, and calculated how many patients improved. Two factors were taken into account.: (1) how statistically reliable the change is by calculating a reliable change index, and (2) how the individual post-treatment score of our dysfunctional patient sample relates to a representative functional group by calculating a cut-off point [48,49]. Although there is no consensus about which method should be reported based on clinically significant change, we based our statistical analysis on the frequently used formulas of Jacobson [51,52]:

(1) We calculated a reliable change index (RCI) for each patient, based on the formula: $RCI = (X_{post} - X_{pre})/S_{diff}$. S_{diff} is calculated with the formula $\sqrt{2}(SE)^2$, where SE=standard error of measure=$SD\sqrt{1-r_{test\text{-}retest\ reliability}}$. When the RCI >1.96 ($p<.05$), we may consider the post-treatment score is representing real, reliable change. For fatigue severity, there was a reliable change when RCI<-1.96, because here lower scores mean more function whereas higher scores indicate less function (or more dysfunctionality).

(2) We calculated cut-off points for the variables of interest: acceptance, PQoL/MQoL, and fatigue. As we had no healthy reference groups with which to compare acceptance (ICQ), PQoL (SF-36), MQoL (SF-36), and fatigue (CIS), we

used the formula: a = M_{pre} + ($2SD_{pre}$). We inverted the direction ($-2SD_{pre}$) for fatigue. This resulted in the following cut-off points: 18.43 (ICQ acceptance), 87.52 (MQoL), 52.83 (PQoL), and 5.33 (fatigue).

When the clinical change is statistically reliable (i.e., not occurring by measurement error) and the cut-off point at the post-treatment measurement is crossed, patients might be considered as 'recovered' on that variable. When clinical change is statistically reliable but the post-treatment score does not cross the cut-off point, patients are considered 'improved'. Finally, when the clinical change is statistically reliable in the negative direction, patients are considered 'deteriorated'.

Correlation and regression analyses

We correlated (Pearson correlations) the change in score with baseline measures ($fatigue_{pre}$, $acceptance_{pre}$ and $neuroticism_{pre}$), and the change in the variables ($MQoL_{change}$, $PQoL_{change}$, $fatigue_{change}$ and $acceptance_{change}$).

In a regression analysis, we explored the unique role of acceptance at baseline in predicting change beyond the effect of neuroticism. For that purpose, only those variables with a significant correlation were used. We used 'enter' as the inclusion method with $MQoL_{change}$ as the dependent variable, and baseline neuroticism (step 1) and acceptance (step 2) as the independent variable.

Results

Patient characteristics

The mean age in our sample (73 women and 7 men) was 43.15 years (SD= 8.54, range=24-57 years). We compared the data regarding the study variables of this sample with an independent sample of 117 non-treated CFS patients (collected during the diagnostic screening on CFS) [25]. Mean fatigue $severity_{pre}$ was 6.43 (SD=0.55) comparable to the mean fatigue in the independent sample (M=6.37, SD=.76). The mean of $acceptance_{pre}$ (M=11.73, SD=3.35) was also comparable (previous sample: M=11.97, SD=3.49). The $neuroticism_{pre}$ mean score was 36.29 (SD=8.79) in this sample, 36.90 (SD=8.63) in our previous sample. The summary scores of the SF-36 were also similar: MQoL (previous sample): 49.41 (SD=17.89), our sample: 50.98 (SD=18.27), PQoL (previous sample: 31.58 (SD=12.52), our sample: 30.03 (SD=11.40).

Pre-post CBT results

Relating to statistical significance, patients reported more acceptance during the post-treatment phase (M=13.91, SD= 3.71) than during the pre-treatment phase (M=11.73, SD=3.35, *t*(79)= 5.72, p<.001). Also fatigue severity showed a significant improvement (*t*(79)= -4.59, p<.0001) from pre to post-treatment. MQoL (t(79)= 3.47, p<.001) and PQoL (t(79)= 3.42, p<.001) also showed a significant improvement (Table 1).

Relating to the practical significance, the effect size (Cohen's d) was moderate for acceptance (0.61) and fatigue severity (-0.56) but small for MQoL (0.37) and PQoL (0.34) (Table 1).

Relating to clinically significant change, our sample (n=80) showed 16 patients who had a reliable change ('improved') in MQoL, but none crossed the cut-off point of 87.52 and could, therefore, be considered recovered. Four patients showed a deterioration in MQoL. PQoL was improved for 21 patients, with 6 recovered. Seven patients showed deterioration in PQoL. We found that fatigue severity improved for 32 patients, recovery was found in 13 patients, 8 patients became worse. For acceptance, 19 patients reported improvement with 4 crossing the cut-off point. Two patients had a reliable change in the negative direction ('deterioration'), and had worse acceptance after treatment (Table 2).

Correlation and regression analyses

$Acceptance_{pre}$ was negatively correlated with $MQoL_{change}$ (r= -0.32, p<.01) and $acceptance_{change}$ (r= -0.40, p<.01), but not with $PQoL_{change}$ (r= -0.03) or $fatigue_{change}$ (r= 0.10). $Neuroticism_{pre}$ showed a significant positive relationship with $MQoL_{change}$ (r=.27, p<.05), but not with $PQoL_{change}$ (r= 0.09), $fatigue_{change}$ (r= -0.16), or $acceptance_{change}$ (r= 0.03). $Fatigue_{pre}$ showed no significant correlations with change variables. Based upon this pattern of correlation, we only performed a regression analysis with $MQoL_{change}$ as outcome.

In the regression analysis with $MQoL_{change}$ as the dependent variable, we found that $neuroticism_{pre}$ had a significant contribution for 7% (β=0.27, Fchange (1,78)=5.88, p< .05, R^2change= 0.07). However, $neuroticism_{pre}$ was no longer significant when $acceptance_{pre}$ was entered. $Acceptance_{pre}$ accounted for 5% additional variance in explaining $MQoL_{change}$ (β= -0.26, p<.05, Fchange (1,77)=4.59, p< .05, R^2change= 0.05). The final model explained 10 % of the variance of $MQoL_{change}$ (adjusted R^2=0.10, F (2,77)=5.37, p<.01) and was significant (p<.05) (Table 3).

Discussion

The primary goal of this study was to evaluate whether acceptance and neuroticism measured during pre-treatment was predictive of improvement in mental and physical QoL and fatigue for patients with CFS who followed a CBT treatment. We first focus upon the extent of improvement due to cognitive behaviour group therapy (CBT) and, then, focus upon whether improvement was affected by initial levels of acceptance and neuroticism.

Overall, the pattern of results in our study indicates that CBT leads to an improvement of mental and physical wellbeing, fatigue and acceptance. For acceptance and fatigue, the effect size was moderate, for QoL the effect sizes are small, which is comparable to the effect sizes reported in the meta-analysis of Castell et al. [10]. Although our results corroborate the overall consensus that CBT is an evidence-based treatment for CFS, its effects are not the same for all patients. CBT seems to produce variable effects both in terms of how many patients benefit from treatment, and in terms of the extent of change experienced. There was a clinical improvement (statistically reliable changes taken the measurement error into account) in all variables of interest for 20% up to 40% of the patients. For example, 40% of the patients showed improvement in fatigue, but fatigue became worse after treatment in 10%. Only 16,3% of the patients could be classified as recovered according to our criteria, which is in line with previous research [55]. The findings for acceptance and physical QoL are less favourable but similar. For mental QoL, only 20% of patients reliably improved, whereas none could be classified as recovered. Analyzing data using criteria of clinical significance reveals a far more nuance picture than the often used statistical criteria. CFS is a chronic condition, and seems to remain a chronic condition for many, even after CBT. It is worth keeping the following two remarks in mind when interpreting the above criteria. First, although one may easily attribute the here observed changes to CBT, one should be careful in doing so. Our study did not include a no-treatment control group. It may thus be possible that natural variation in outcomes occurs independently of treatment [56]. Second, a focus upon clinical significance is much needed in evaluating treatment efficacy and effectiveness, but finding a clear-cut criterion for recovery is an hazardous enterprise in chronic conditions. More research is needed to define exactly what is meant by recovery, and to provide data from which clinical cut-offs can be derived. Moreover, we have to keep in mind that patients scoring their QoL after treatment is closely related to their operationalization of the concept of 'recovery', this operationalization can change eventually during psychological treatment [4,56]. Despite these considerations our results show the least clinical significant change in

mental and physical QoL, which may suggest that we have to focus more on other factors to enhance a better QoL.

Despite the good evidence base for CBT, more research is needed to understand for whom CBT is effective and how exactly the change in CBT is accomplished [57]. Therefore, an important challenge is not to identify whether CBT works, but for *whom* CBT works. In our study we addressed this issue by exploring whether acceptance and neuroticism at baseline were predictive of change after CBT. We observed that these variables were predictive of changes in mental QoL. Low levels of acceptance, and high levels of neuroticism at baseline were associated with a larger improvement in mental QoL. This is remarkable. One may easily believe that those low in acceptance and high on neuroticism would benefit less from a group therapy focused upon the improvement of functioning because clinically, the improvement in mental QoL of more neurotic patients is not always clear because those patients remain reporting a lower mental QoL before and after treatment in comparison with the patients scoring lower on neuroticism [31]. The reverse seems to be the case in our study. We suspect that several aspects of the treatment (structure of the programme, activity management, psycho-education on CFS and stress, and stress-management) effectively diminish a dominant focus on symptoms, extinguish avoidance, and also stimulate acceptance [12-14]. These findings are encouraging for therapists who work with this type of patients. Moreover, the results suggest that we have to keep in mind that patients with low acceptance and a neurotic personality should not be excluded, and can benefit from a group CBT programme [58].

Of further note in this context is that acceptance seems to be more important than neuroticism. Acceptance at baseline had a unique role in predicting changes in mental QoL beyond the effect of neuroticism. Our results indicate that there is need for more systematic focus on acceptance in the psychological assessment before treatment in this population. This is well in line with research in chronic pain: improving acceptance is considered as more important than other coping strategies to achieve treatment success [59-64]. It may well be that a more explicit focus on acceptance will also prove beneficial for patients with chronic fatigue syndrome. Low acceptance at baseline can be considered as an extra indication for group CBT treatment because of its impact on QoL, provided the therapeutic goal of the CBT broadens from only focussing on decreasing the fatigue (curing) to also focussing on ‘a better QoL’ (caring). As yet, research on the role of acceptance in CFS is limited. Only a few studies has examined acceptance as predictor of health-related quality of life, and one recent study emphasized the importance of acceptance within a treatment of CFS patients [15]. More

research is required to provide therapists and researchers more insight into the role of acceptance in treatment.

Of further interest is that although our treatment did not include specific acceptance interventions, acceptance was improved. A clinically relevant improvement in acceptance for nearly a quarter of the patients (23.8%) suggests that traditional, group cognitive-behavioural interventions can influence the process of acceptance. Along this line, a study in chronic pain patients also showed statistically significant and clinical changes in acceptance after traditional CBT [65]. The fact that acceptance may be improved despite not being an explicit treatment target, may explain why Hofmann et al. observed that acceptance-orientated treatments (ACT and Mindfulness) do not result in better results than cognitive behaviour therapy (CBT) [66]. Interventions targeting acceptance may be consistent with and complementary to a CBT approach [66]. A remaining challenge will be to refine CBT in order to improve its effects. We present here some ideas: (1) specific *educational elements* concerning acceptance; (2) more focus on *cognitive reframing* provided it is within a context of accommodative coping; (3) stimulating *behavioural experiments* in which an acceptance is central. However, we acknowledge that in order to realise these objectives, therapists need to have the appropriate therapeutic skills and competences. Additional research will be important to investigate what is necessary to enhance the impact of acceptance and to refine CBT interventions accordingly.

We conclude that the strength of this study lies in the fact that the results contribute to a better estimation of which patient characteristics predict the improvement by CBT. Although acceptance and neuroticism at baseline explained only about 10% of the variance of change in mental health quality of life, these findings gives support to the idea that these characteristics have to be considered with regard to psychological treatment for CFS patients. Which cognitive behavioural therapeutic factors are effective and responsible for these findings remains to be investigated, but systematically assessing acceptance and personality characteristics before and after treatment can initiate research on appropriate psychotherapeutic interventions. Furthermore, we have shown that, although neuroticism might be high, CBT has an effect on mental QoL. This may have an impact on the screening of patients who are eligible for these treatment programmes. Whether it is more efficient to divide the groups (more and less neurotic) has to be considered and addressed in further research on this matter. Another consideration might be to provide a more tailored group programme, which might mean a longer duration of therapy. In the meta-analysis of Castell et

al. the number of treatment hours was indeed shown to be a significant predictor of the effect of CBT [10]. Research on this possible association is required.

There are some limitations to this study. First, we do not have a control group; it is therefore unclear whether changes experienced by patients resulted from the CBT treatment, natural evolution, or other variables. A control group could have given the study more strength. However, a control group with an indication for the group therapy which did not receive the therapy, was not possible in our service. Second, we couldn't not perform analyses to compare the patients who dropped out before ending the group therapy and those who completed the programme. These analyses would have been interesting with regard to the impact of personality characteristics on drop out and to generalize our findings. Third, more adequate data in the literature for calculating clinical significant cut-off points should be encouraged. It might also be that the clinically change results are underestimated because of the stringent cut-off points. This is especially true for patients with chronic illnesses such as CFS, in which a full 'recovery' based on crossing the cut-off is often difficult to achieve [8]. Fourth, the size of our sample is appropriate and comparable with other studies, but still not large (n=80). Fifth, studies on the mediating effect of acceptance change and long-term follow-up are recommended to provide more insight on the impact of change in acceptance on QoL improvement.

Acknowledgments

We want to thank Mrs I. Vandereyden and the fellow psychologists of the outpatient clinic of the General Internal Medicine department of the Ghent University Hospital for their help in data collection for this study.

Conflict of interest

The authors have no competing interests to report.

Role of the funding source

The realization of this manuscript was supported by a ‘Special PhD scholarship’ of the Research Foundation Flanders to Carine Poppe.

References

1. Fukuda K, Straus S, Hickie I, Sharpe M, Dobbins J, Komaroff A. The chronic fatigue syndrome: a comprehensive appoach to its definition and study. Annals of Internal Medicine 1994; 121:953-959.
2. Diagnostic and Statistical Manual of Mental Disorders, Version IV.
3. Surawy C, Hackmann A, Hawton K, Sharpe M. Chronic fatigue syndrome: a cognitive approach. Behavioural Research Therapy 1995; 33:535-544.
4. Prins J, van der Meer J, Bleijenberg G: Chronic fatigue syndrome. Lancet 2006; 367:346-355.
5. Kato K, Sullivan P, Evengärd B, Perdersen N: Premorbid predictors of chronic fatigue. Arch Gen Psychiatry. 2006; 63:1267-1272.
6. Deary V, Sharpe M. The cognitive behavioural model of medically unexplained symptoms: a theoretical and empirical review. Clin Psychology Review 2007; 27: 781-797.
7. Tak L, Rosmalen J. Dysfunction of stress respons systems as a risk for functional somatic syndromes. Journal of Psychosomatic Research 2010; 68:461-468.
8. Wyller V. The chronic fatigue syndrome-an update. Acta Neurologica Scandinavica. 2007; 115:7-14.
9. White P, Goldsmith K, Johnson A, Potts L, Walwyn R, DeCesare J, Baber H, Burgess M, Clark L, Cox D, Bavinton J, Angus B, Murphy G, Murphy M, O'Dowd H, Wilks D, McCrone P, Chalder T, Sharpe M, on behalf of the PACE trial management group. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Lancet 2011; 377:823–836.
10. Castell B, Kanzantzis N, Moss-Morris R. Cognitive Behavioral Therapy and Graded Exercise for Chronic Fatigue Syndrome: A Meta-Analysis. Clin Psychology: Science and practice 2011; 18:311-324.
11. Cohen J. Statistical power analysis for the behavioral sciences. 1988, 2nd ed. Hillsdale, NJ: Erlbaum
12. Wiborg J, Knoop H, Prins J, Bleijenberg G. Does a decrease in avoidance behavior and focusing on fatigue mediate the effect of cognitive behavior therapy for chronic fatigue syndrome? Journal of Psychosomatic Research 2011; 70(4):306-310.
13. Prins J, Bleijenberg G, Bazelmans E, et al. Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. Lancet 2001; 357:841–847.
14. Cella M, Chadler T, White P: Does the heterogeneity of chronic fatigue syndrome moderate the response to cognitive behaviour therapy? An exploratory study. Psychotherapy and Psychosomatics 2011; 80:353-358.
15. Brooks S, Rimes K, Chadler T. The role of acceptance in chronic fatigue syndrome. Journal of Psychosomatic Research 2011; 71(6):411-415.
16. Evers A, Kraaimaat F, van Lankveld W, Jongen P, Jacobs J, Bijlsma J. Beyond unfavorable thinking: The Illness Cognition Questionnaire for Chronic Diseases. Journal of Consulting and Clinical Psychology 2001; 69:1026-1036.
17. Compas B, Jaser S, Dunn M, Rodriguez E. Coping with Chronic Illness in Childhood and Adolescence. Annual Review of Clinical Psychology 2012; 8:455–80.
18. Karademas E, Hondronikola I. The impact of illness acceptance and helplessness to subjective health, and their stability over time: a prospective study in a sample of cardiac patients. Psychology Health & Medicine 2010; 15 (3): 336-346.
19. Aldwin C, Park C. Coping and physical health outcomes: An overview. Psychology and Health 2004; 19(3): 277-281.

20. Nakamura Y, Orth U. Acceptance as a coping reaction: Adaptive or not? Swiss Journal of Psychology 2005; 64(4):281-292.
21. Kranz D, Bollinger A, Nilges P. Chronic pain acceptance and affective well-being: A coping perspective. European Journal of Pain 2010;14(10):1021-1025.
22. Vriezekolk J, Geenen R, van den Ende C, Slot H, van Lankveld W, van Helmond T. Behavior change, acceptance, and coping flexibility in highly distressed patients with rheumatic diseases: Feasibility of a cognitive-behavioral therapy in multimodal rehabilitation. Patient Education and Counseling 2012; 87: 171–177.
23. Maes S, Karoly P. Self-regulation assessment and intervention in physical health and illness: a review. Appl Psychol Intern Rev 2005; 54(2):267-299.
24. Carver C, Scheier M. On the self-regulation of behavior. New York: Cambridge University Press 1998.
25. Wrosch, C., Scheier, M.F., Miller, G.E., Schulz, R., Carver, C.S. (2003). Adaptive self-regulation of unattainable goals: Goal disengagement, goal reengagement, and subjective well-being. Personality and Social Psychology Bulletin,29,1494-1508. doi: 10.1177/0146167203256921
26. Brandtstädter J, Renner G. Tenacious goal pursuit and flexible goal adjustment: explication and age-related analysis of assimilative and accommodative strategies of coping. Psychol Aging 1990; 5:58–67.
27. Brandtstädter J. Goal pursuit and goal adjustment: self-regulation and intentional self-development in changing developmental contexts. Advances in Life Course Research 2009; 14: 52–62.
28. Lauwerier E, Crombez G, Van Damme., Goubert L, Vogelaers D, Evers A. The Construct Validity of the Illness Cognition Questionnaire: The Robustness of the Three-factor Structure Across Patients with Chronic Pain and Chronic Fatigue. International Journal of Behavioural Medicine 2010; 17:90–96.
29. Söderberg S, Evengard B. Short-term Group therapy for Patients with Chronic Fatigue Syndrome. Psychotherapy and Psychosomatics 2001; 70:108-111.
30. Dickson A, Knussen C, Flowers P. 'That was my old life; it's almost like a past-life now: identity crisis, loss and adjustment amongst people living with CFS. Psychology and Health, 2008;23, 459-476.
31. Poppe C, Crombez G, Hanoulle I , Vogelaers D, Petrovic M. Mental Quality of Life in Chronic Fatigue Is Associated with an Accommodative Coping style and Neuroticism: A Path Analysis. Quality of life Research, 2012; 21(8):1337-1345.
32. Carver C, Connor-Smith J. Personality and coping. Annual Review Psychology 2010; 61: 679-704.
33. Ormel J, Riese H, Rosmalen J. Interpreting neuroticism scores across the adult life course: immutable or experience-dependent set points of negative affect? Clin Psychology Review 2012;32:71-79.
34. Nater U, Jones F, Lin J, Maloney E, Reeves W, Heim C. Personality features and Personality disorders in Chronic Fatigue Syndrome: A Population-based Study. Psychotherapy and Psychosomatics 2010; 79:312–318.
35. Hardt J, Buchwald D, Wilks D, Sharpe M, Nix W, Egle U. Health-related quality of life in patients with chronic fatigue syndrome: An international study. Journal of Psychosomatic Research, 2001;51:431-4.
36. Rakib A, White P, Pinching A, Hedge B, Newbery N, Fakhoury W, Priebe S. Subjective quality of life in patients with chronic fatigue syndrome. Quality of Life Research 2005;14:11-19.
37. Anderson J, Ferrans C. The quality of life of persons with chronic fatigue syndrome. Journal of Nervous and Mental Disease 1997;185:359-67.

38. Johnson S, Deluca J, Natelson B. Personality dimensions in the chronic fatigue syndrome: a comparison with mutiple sclerosis and depression. Journal of Psychiatric Research 1996;30: 9-20.
39. Goodwin R, Engstrom G. Personality and the perception of health in the general population. Psychological Medicine. 2002; 32:325-332.
40. Van Damme S, Crombez G, Van Houdenhove B, Mariman A, Michielsen W. Well-being in patients with chronic fatigue syndrome: the role of acceptance. J of Psychosomatic Research 2006,61:595-599.
41. Bazelmans E, Prins J, Bleijenberg G. Cognitive behavior therapy for relatively active and for passive chronic fatigue syndrome patients. Cognitive Behavioural Practice, 2006;13,157-66.
42. Ware J, Sherbourne C. The medical outcomes study 36-item short form health survey (SF-36): Conceptual framework an item selection. Medical Care 1992; 30:473-483.
43. Aaronson N, Muller M, Cohen P, Essink-Bot M, Fekkes M, Sanderman R, Sprangers M, teVelde A, Verrips E. Translation, validation and norming of the dutch language version of the SF-36 Health Survey in community and chronic disease populations. Journal of Clinical Epidemiology 1998; 51(11): 1055-1068.
44. Vercoulen J, Swanink C, Fennis J, Galama J, van der Meer J, Bleijenberg G. Dimensional assessment of chronic fatigue syndrome. Journal of Psychosomatic Research 1994; 38:383-392.
45. De Fruyt F, Mervielde I. The assessment of the big five in the Dutch language domain. Psychologica Belgica 1998; 38:1-22.
46. Costa P, McCrae R. Personality disorders and the five factor model of personality. Journal of Personality Disorders 1990; 4:362-371.
47. Shearer-Underhill C, Marker C. The use of the number needed to treat in randomized controlled trials in psychological treatment. Clinical Psychology: Science and Practice. 2010;17:41-47.
48. Conner B. When is the difference significant? Estimates of meaningfulness in clinical research. Clinical Psychology: Science and Practice 2010; 17:52-57.
49. Morley S. Efficacy and effectiveness of cognitive behavioural therapy for chronic pain: progress and some challenges. Pain 2011; 152:99-106.
50. Field A. Discovering statistic using SPSS, Third edition. Sage publications 2009.
51. Jacobson N, Truax P: Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. Journal of Consulting and Clinical Psychology. 1991; 59(1):12-19.
52. Jacobson N, Roberts L, Berns S, McGlinchey J. Methods for defining and determining the clinical significance of treatment effects: description, application and alternatives. J of Consulting and Clinical Psychology. 1999; 67(3):300-307.
53. Dunlap W, Cortina J, Vaslow J, Burke M. Meta-analysis of experiments with matched groups or repeated measures designs. Psychological Methods 1996 (2):170-177.
54. Borenstein M, Hedges L, Higgins J, Rothstein H. Introduction to Meta-analysis. West Sussex, Wiley 2009.
55. Knoop H, Bleijenberg G, Gielissen M, van der Meer J, White P. Is a full recovery possible after cognitive behavioural therapy for chronic fatigue syndrome? Psychotherapy and Psychosomatics 2007; 76:171-176.
56. Heins M, Knoop H, Prins J, Stulemeijer M, van der Meer J, Bleijenberg G. Possible detrimental effects of cognitive behaviour therapy for chronic fatigue syndrome. Psychotherapy and Psychosomatics 2010; 79:249-256.
57. Knoop H. Cognitive Behavior Therapy for chronic fatigue syndrome: Where to go from here? Clinical Psychology Science and Practice 2011; 18: 325–330.

58. Van Geelen S, Sinnema G, Hermans H, Kuis W. Personality and chronic fatigue syndrome: methodological and conceptual issues. Clinical Psychology Review. 2007; 27:885-903.
59. McCracken L, Eccleston C. A comparison of the relative utility of coping and acceptance-based measures in a sample of chronic pain sufferers. European Journal of Pain 2006; 10:23-29.
60. McCracken L, Vowles K, Gauntlett-Gilbert J. A Prospective Investigation of Acceptance and Control-Oriented Coping with Chronic Pain. Journal of Behavioural Medicine 2007; 30:339–349
61. Vowles K, McCracken L. Acceptance and values-based action in chronic pain: A study of treatment effectiveness and process. Journal of Consulting and Clinical Psychology 2008; 76: 397-407.
62. Samwel H, Kraaimaat F, Crul B, van Dongen R, Evers A. Multidisciplinary allocation of chronic pain treatment: Effects and cognitive-behavioural predictors of outcome.British Journal of Health Psychology 2009; 14: 405-421.
63. Thompson M, McCracken L. Acceptance and Related Processes in Adjustment to Chronic Pain. Current Pain and Headache Reports, 2011; 15 (2): 144-151.
64. Blacker K, Herbert J, Forman, Evan M, Kounios J. Acceptance-Versus Change-Based Pain Management: The Role of Psychological Acceptance. Behaviour Modification 2012; 36 (1): 37-48.
65. Baranoff J, Hanrahan S, Kapur D, Connor J. Acceptance as a process variable in relation to catastrophizing in multidisciplinary pain treatment. European Journal of Pain. 2012; doi:10.1002/j.1532-2149.2012.00165.x
66. Hofmann S, Sawyer A, Fang A. The Empirical Status of the "New Wave" of Cognitive Behavioral Therapy. Psychiatric Clinics of North America 2010; 33 (3): 701-710.

Table 1. t test of the differences pre- and post CBT (paired).

Variables	Pre-treatment Mean (SD)	Post-treatment Mean (SD)	Treatment effect [95% CI]	Effect size (Cohen's d) [95% CI]
MQoL	50.98 (18.27)	57.20 (14.85)	6.22 [2.65 to 9.79]*	.37 [.15 to .58]
PQoL	30.03 (11.40)	34.23 (12.97)	4.19 [1.75 to 6.63]*	.34 [.14 to .54]
Acceptance	11.73 (3.35)	13.91 (3.71)	2.19 [1.43 to 2.95]**	.61 [.38 to .85]
Fatigue severity	6.43 (.55)	6 (.89)	-.42 [-.61 to -.24]**	-.56 [-.82 to -.31]

*= p<0.001; **=p<0.0001**

Norm Independent Cohen's d: > 0.15 en <0.40 = small effect
> 0.40 en <0.75 = moderate effect
> 0.75 en <1.10 = large effect
>1.10 = very large effect

Table 2. Clinically significant change

Measure	n	Recovered (%)	Improved (%)	Detoriated (%)
MQoL	80	0	16 (20)	4 (5)
PQoL	80	6 (7.5)	21 (26.25)	7 (8.75)
Acceptance	80	4 (5)	19 (23.75)	2 (2.5)
Fatigue	80	13 (16,25)	32 (40)	8 (10)

Recovered = fulfilled both conditions : RCI >1.96 (p<.05) and crossed over the cut-off point
Improved = fulfilled RCI >1.96 (p<.05)
Detoriated = fulfilled RCI >1.96 (p<.05) in negative direction
The 'improved' include the 'recovered'

Table 3. Linear regression analyses with acceptance and neuroticism pre-treatment as independent variables.

Outcome	Predictors	Step	Adj R^2	R^2 Change	B	Beta	P
$MQoL_{change}$	Neuroticism	1	.06	.07*	.28	.15	.21
	Acceptance	2	.10	.05*	-1.22	-.26	.04*

p < .05*