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# The role of the therapeutic relationship in cognitive behaviour therapy for chronic fatigue syndrome

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## ABSTRACT

Cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) can reduce fatigue and impairment. Recently, it was found that changes in fatigue-perpetuating factors, i.e. focusing on symptoms, control over fatigue, perceived activity and physical functioning, are associated with and explain up to half of the variance in fatigue during CBT for CFS. The therapy relationship, e.g. outcome expectations and working alliance, may also contribute to treatment outcome. We aimed to examine the role of the therapy relationship in CBT and determine whether it exerts its effect independently of changes in fatigue-perpetuating factors. We used a cohort of 217 CFS patients in which the pattern of change in fatigue-perpetuating factors was examined previously. Fatigue, therapy relationship and fatigue-perpetuating factors were measured at the start of therapy, three times during CBT and at the end of therapy. Baseline outcome expectations and agreement about the content of therapy predicted post therapy fatigue. A large part of the variance in post-treatment fatigue (25%) was jointly explained by outcome expectations, working alliance and changes in fatigue-perpetuating factors. From this, we conclude that positive outcome expectations and task agreement seem to facilitate changes in fatigue-perpetuating factors during CBT for CFS. It is therefore important to establish a positive therapy relationship early in therapy.

## Abbreviations

CAL, causal attribution list;  
CBT, cognitive behaviour therapy;  
CFS, chronic fatigue syndrome;

CIS, Checklist Individual Strength;  
SF36, Medical Outcomes Survey Short Form 36;  
SIP, sickness impact profile;  
WAI-s, Working Alliance Inventory – Short Form

## INTRODUCTION

Chronic fatigue syndrome (CFS) is characterised by severe and medically unexplained fatigue that lasts longer than 6 months and results in severe limitations in daily life (Fukuda et al., 1994; Reeves et al., 2003). Cognitive behaviour therapy (CBT) for CFS can effectively reduce fatigue and impairment (Castell, Kazantzis, & Moss-Morris, 2011; Chambers, Bagnall, Hempel, & Forbes, 2006; Price, Mitchell, Tidy, & Hunot, 2008). Even full recovery, defined as no longer being severely fatigued, being able to resume all activities, and having a perception of health and fatigue that is similar to healthy persons, is possible for a subgroup of patients (Knoop, Bleijenberg, Gielissen, van der Meer, & White, 2007). Several models underlying CBT for CFS assume that there are certain fatigue-related beliefs and behaviour that perpetuate symptoms (Fry & Martin, 1996; Gaab, 2004; Surawy, Hackmann, Hawton, & Sharpe, 1995; Vercoulen et al., 1998; Wessely, David, Butler, & Chalder, 1989). One of these models is that of Vercoulen et al. (1998). It is the only model that was statistically tested and it states that a high level of somatic attributions and focusing on symptoms and a low level of physical activity and low perceived control over symptoms lead to perpetuation of fatigue.

Recently, Wiborg, Knoop, Prins & Bleijenberg (2011); Wiborg, Knoop, Frank & Bleijenberg (2012); Wiborg, Knoop, Stulemeijer et al. (2010) used mediation analyses of previous randomised controlled trials (RCTs) to test whether 1) CBT indeed leads to a change in these fatigue-perpetuating factors and 2) whether this change was related to the reduction in fatigue. Their studies showed that changes in focusing on symptoms and sense of control over fatigue indeed mediate the change in fatigue during CBT for CFS (Wiborg, Knoop, et al., 2012; Wiborg, et al. 2011). However, it is not the actual change in physical activity, but the perceived increase in activity that mediates the decrease in fatigue (Wiborg, Knoop, et al., 2012; Wiborg, Knoop, Stulemeijer, Prins, & Bleijenberg, 2010). Heins et al. furthered their work by studying how these fatigue-perpetuating factors change during CBT for CFS. Their study showed that these variables change in the same period in which fatigue decreases. Changes in fatigue-perpetuating factors explained up to half of the variance in fatigue during CBT for CFS (Heins et al. submitted for publication). So although these studies provided insight into the changes that lead to a decrease in fatigue, these changes could only partly explain the treatment outcome of CBT for CFS.

Besides specific treatment techniques, extant research suggests that the therapy relationship, i.e. “the feelings and attitudes that therapist and client have toward one another and how these are expressed” (Norcross, 2001), is also an important contributor to treatment outcome in a variety of psychotherapies. A recent task force on evidence-based therapy relationships even concluded that “the therapy relationship accounts for why clients improve (or fail to improve) at least as much as

the particular treatment method” (Norcross & Wampold, 2011). Wampold and Budge recently proposed a model of the therapy relationship, which consists of the bond between patient and therapist, setting of goals and tasks and expectations with respect to treatment outcome (Wampold & Budge, 2012). This model thus includes outcome expectations and three elements of the working alliance as proposed by Bordin: task, goal and bond (Bordin, 1979). Tasks are what therapist and patient agree that needs to be done to reach the patient's goals. Goals are what the patient hopes to gain from therapy. Bond is the trust and confidence in the therapist. Although both outcome expectations and working alliance are considered empirically supported relational attributes across studies of various therapies (Constantino, Arnkoff, Glass, Ametrano, & Smith, 2011; Fluckiger, Del Re, Wampold, Symonds, & Horvath, 2012; Horvath, Del Re, Fluckiger, & Symonds, 2011), their application is developed and maintained in different ways within different therapeutic models and protocols (Hatcher & Barends, 2006; Ulvenes et al., 2012; Wampold & Budge, 2012). We'll therefore briefly discuss the application of outcome expectations and working alliance in CBT in general and CBT for CFS specifically. In the protocol used for this study, recovery is considered the highest achievable outcome of CBT. Patients, however, may be hesitant to believe that full recovery is possible and may only expect to learn to cope with their chronic fatigue. Both the aetiology of CFS and its treatment are hotly debated (Action for ME/Association of Young People with ME, 2008; Kean, 2010; Working group on CFS/ME (Chronic Fatigue Syndrome/Myalgic Encephalomyelitis), 2002). Many CFS patients attribute their symptoms to a physical cause, such as a viral infection or immunological disorder (Deale, Chalder, & Wessely, 1998). Patients with strong somatic attributions will, understandably, not immediately have faith in a cognitive behavioural therapist and the rationale of CBT. Indeed, the placebo response, which is strongly related to outcome expectations (Di Blasi, Harkness, Ernst, Georgiou, & Kleijnen, 2001), is lower in psychological interventions for CFS than in somatic interventions (Cho, Hotopf, & Wessely, 2005). Furthermore, in a recent large RCT only 57% of the CFS patients allocated to CBT indicated that they were confident about the treatment (White et al., 2011). The fact that patients are often referred for CBT after they have had symptoms for several years (see for example the study of Prins et al. (2001) with a median symptom duration of 4.9 years) may further lower outcome expectations. The working alliance in CBT is mainly reflected in collaborative empiricism, i.e. patient and therapist collaborating to uncover negative automatic thoughts through Socratic reasoning and homework assignments (Dattilio & Hanna, 2012). Although in the theory underlying CBT it is assumed that a good working alliance in itself is insufficient to bring about change (Clark, Beck, & Alford, 1999), a good alliance is considered necessary and has been related to positive treatment outcome (Horvath et al., 2011). The working alliance in CBT for CFS may not always be good as some CFS patients will have a different view than the CBT therapist about the cause of CFS (e.g. a somatic versus a cognitive behavioural model of CFS) and the goal of treatment (e.g. recovery versus coping with a chronic illness). The first objective of this paper is to determine whether outcome expectations and working alliance contribute to the reduction in fatigue during CBT for CFS. A second objective is to determine whether they have a direct effect on treatment outcome, independently of

changes in fatigue-perpetuating factors or exert their effect (also) indirectly through changes in fatigue-perpetuating factors.

## **METHODS**

### **Patients**

We assessed the effect of the therapeutic relationship in the same cohort of patients in which the pattern of change in fatigue-perpetuating factors was previously examined (Heins et al., submitted for publication). In this study, consecutively referred patients who started CBT at our tertiary CFS specialist care centre between April 2008 and September 2010 were eligible to participate if they:

- Met the criteria for CFS as stated by the US Centers for Disease Control and Prevention. These include the experience of severe and medically unexplained fatigue for at least six months that brings about severe impairment in daily living and is accompanied by four out of eight specific additional symptoms (Fukuda et al., 1994; Reeves et al., 2003). These are by far most often used in studies on CFS (Christley, Duffy, & Martin, 2012). Severe fatigue was defined as a score of  $\geq 35$  on the Checklist Individual Strength (CIS), subscale fatigue severity (Vercoulen et al., 1994), and severe functional impairment was defined as a total score  $\geq 700$  on the Sickness Impact Profile (SIP) (Bergner, Bobbitt, Pollard, Martin, & Gilson, 1976; Jacobs, Luttik, Touw-Otten, & de Melker, 1990; Knoop et al., 2007; Pollard, Bobbitt, Bergner, Martin, & Gilson, 1976). If patients had not been extensively medically examined prior to referral, they first received a standard medical examination at the outpatient clinic of our department of internal medicine, to rule out any somatic disorder that excludes the diagnosis of CFS.
- Were at least 18 years old. There is a separate treatment protocol for adolescent patients at our centre.
- Were able to read and write Dutch.

Patients were excluded if they were currently engaged in a legal procedure for a disability claim until this procedure was completed.

The study was conducted according to the Helsinki declaration as revised in 1994, and approved by the ethical committee of the Radboud University Nijmegen Medical Centre. All participants gave written informed consent before participation.

### **CBT**

The protocol of CBT for CFS used in this study (Bleijenberg et al., 2003; Knoop & Bleijenberg, 2010) consists of approximately 12 sessions during 6 months. First of all, illness attributions are discussed with the patient, bearing in mind that a somatic cause for the symptoms has not been found in previous medical examination. The way through which thoughts and behaviour can lead to the persistence of symptoms is explained and the patient formulates his or her goals of therapy. These goals usually include the resumption of work, hobbies and other activities that imply recovery for the patient. Recovery is named as the maximal attainable goal of therapy, although patients are told that not every patient will reach this goal. After

the formulation of treatment goals, bedtimes are regulated to stop disruption of the circadian rhythm. Next, patients are taught how to recognise and challenge non-accepting and catastrophising thoughts in response to fatigue that may hamper adequate coping. They also learn to redirect their attention from the fatigue to activities and their environment. Patients who are relatively physically active (i.e. bursts of activity followed by inactivity) first start dividing their activity evenly throughout the day. Patients who have a low level of physical activity start immediately with the next part of the treatment, in which patients gradually increase their level of physical activity, mostly by walking or cycling. Dysfunctional illness beliefs, such as the thought that even moderate levels of activity are harmful, are challenged during this period. Once patients have increased their level of physical activity, they start to realise their treatment goals in the same way. At the end of treatment they are encouraged to stop labelling themselves as a CFS patient. All participating therapists were thoroughly trained in the protocol of CBT for CFS and received frequent intervision and supervision to ensure fidelity to the treatment protocol.

### **Measurements**

Baseline and post-treatment fatigue were measured as a part of the standard diagnostic procedure at our centre. Baseline expectations and working alliance were assessed after the first therapy session, to ascertain that a baseline working alliance could have been established. As changes in outcome expectations and alliance after the first session may also affect treatment outcome, we conducted three interim measurements of fatigue, expectations and working alliance: 6, 12 and 18 weeks after the start of CBT. Patients received the questionnaires from the researcher and were told that their answers would not be communicated with their therapist. This was also mentioned in the written information about the study and in the written instructions given together with the questionnaires. Patients were informed that the study aimed to investigate how CBT for CFS works.

### **Fatigue**

Fatigue was assessed with the subscale fatigue severity of the Checklist Individual Strength (CIS). This subscale indicates the level of fatigue in the previous two weeks, measured with eight items on a seven-point scale (range 8–56). A score of 35 and higher (i.e. 2 standard deviations above the mean of a healthy control group) indicates severe fatigue. Cronbach's alpha ranges from 0.83 to 0.92 (Vercoulen, Alberts, & Bleijenberg, 1999; Vercoulen et al., 1994).

### **Baseline characteristics**

#### *Somatic attributions*

Somatic attributions regarding the CFS symptoms were measured with the Causal Attributions List (CAL), which consists of five questions measured on a five-point Likert scale (range 5–20). Higher scores indicate more somatic attribution (Prins et al., 2001).

#### *Limitations in daily functioning*

Limitations in daily functioning were measured with the Sickness Impact Profile (SIP), (Bergner et al., 1976) which is a widely used multi-facetted questionnaire with

good reliability (Pollard et al., 1976). It measures limitations on different domains of daily living, such as sleep and rest, work, home management, mobility and social interaction. It has been repeatedly used in studies testing the efficacy of interventions for CFS. A score above 700 indicates severe limitations (van der Werf, de Vree, Alberts, van der Meer, & Bleijenberg, 2002).

## **Therapy relationship**

### *Outcome expectations*

Patients' expectations about the outcome of therapy were measured with the Treatment Outcome Expectations Questionnaire, which was developed for this study. The original questionnaire consisted of 5 questions regarding expectations with respect to the outcome of the treatment: 1) Treatment will help me to get rid of my symptoms; 2) After treatment I will be less fatigued; 3) I'll learn to cope with my fatigue; 4) I'll learn to accept my fatigue; 5) After treatment I'll be recovered. These questions were answered on a four point Likert-scale ranging from 'I do not expect that at all' (0) to 'I most certainly expect that' (4). Higher scores indicate more positive outcome expectations. Therapists' expectations about the outcome of therapy were measured with the following question: 'Do you think that [name of patient] will be recovered after therapy?' Therapists answered this question on a 100 mm Visual Analogue Scale ranging from 'certainly not' (0) to 'most certainly' (100).

### *Working alliance*

Working alliance was measured with the Working Alliance Inventory – Short Version (WAI-S) (Tracey & Kokotovic, 1989). This questionnaire consists of a separate client and a therapist version and measures working alliance using 12 questions on a 5-point Likert scale ranging from 'never' to 'always'. Three subscales can be calculated; bond, goal agreement and task agreement. These subscales reflect the emotional bond with the therapist and the agreement about the goal of therapy and the tasks that have to be performed to reach this goal. Factor analysis showed that these three factors were also valid for the Dutch translation (Stinckens, Ulburghs, & Claes, 2009). These factors are also relevant to our study. The task scale is relevant as patient and therapist may disagree about the content of the therapy, i.e. patients may believe that changing their thoughts and behaviour will not change their fatigue. The goal scale is relevant as patient and therapist may disagree about the goal of therapy, i.e. recovery vs. coping with chronic fatigue. Also the bond scale is useful. As we hypothesized in the introduction, the bond between patient and therapist may be less important in CBT for CFS as patients may see the therapist as someone explaining the treatment, however, this still has to be confirmed. Internal consistency of these factors was 0.85 for the task scale, 0.83 for the goal scale and 0.82 for the bond scale (Stinckens et al., 2009). In our study, this was 0.76, 0.73 and 0.75 respectively.

### *Fatigue-perpetuating factors*

Fatigue perpetuating factors were measured with the same instruments as in the previous study of Heins et al. (submitted for publication). Control over fatigue was measured with the self-efficacy scale (De Vree et al., 2002; Prins et al., 2001)

(Cronbach's alpha 0.68–0.77). Focusing on symptoms was measured with the subscale 'focusing on symptoms' of the Illness Management Questionnaire (Ray, Weir, Stewart, Miller, & Hyde, 1993) (Cronbach's alpha 0.88). Self-perceived physical activity was measured with the Checklist Individual Strength subscale physical activity (Vercoulen et al., 1994). (Cronbach's alpha 0.81) Self-reported physical functioning were measured with the corresponding subscale of the Medical Outcomes Survey SF36 (Steward, Hays, Ware 1998) (Cronbach's alpha 0.91).

### **Statistical analyses**

To determine the psychometric properties of the Treatment Outcome Expectations Questionnaire, a list specifically developed for the current study, we performed an exploratory varimax rotated factor analysis and determined internal consistency of the obtained factors.

To test whether baseline expectations and working alliance predicted treatment outcome we built a multilevel linear regression model. Therapist was defined as the second level, and patient as the first level. For these analyses, we selected all patients who had completed the post-treatment measurement. We used a stepwise approach in which we started with a null-model with post-treatment fatigue as dependent variable and the baseline characteristics fatigue, symptom duration, somatic attributions and physical functioning as independent variables. These baseline characteristics were hypothesized to either predict treatment outcome (baseline fatigue and physical functioning) or to be related to the therapy relationship (symptom duration and somatic attributions). In the second step we then added outcome expectations and working alliance of the patient, in the third step we added outcome expectations and working alliance as rated by the therapist. Using an *F*-test, we could statistically test the incremental proportions of variance in post-treatment fatigue attributable to each set of variables.

As changes during therapy may also affect the outcome of CBT, we also tested whether changes in outcome expectations and working alliance predicted post-treatment fatigue. We built separate multilevel linear regression models for each period (e.g. baseline – first interim measurement) in a stepwise approach similarly to that described for the pre-treatment variables in the previous paragraph. We first entered the significant baseline predictors of post-treatment fatigue and values of outcome expectations and working alliance at the start of the period, as a second step we entered the change in outcome expectations and working alliance during the period as rated by the patients and as a third step as rated by the therapists.

Finally, we assessed the amount of variance in post-treatment fatigue explained by the therapy relationship and fatigue-perpetuating factors. As a first step we built a model with only those variables that significantly predicted post-treatment fatigue. We first entered baseline characteristics, then outcome expectations and working alliance at baseline, changes in outcome expectations and working alliance were entered as a separate step for each period, and finally we added the total change during therapy in fatigue-perpetuating factors that had previously been found to mediate the treatment effect of CBT for CFS (control over fatigue, focusing on

symptoms, self-perceived physical activity and physical functioning). The proportion of variance in post-treatment fatigue each step explained independently was tested with an *F*-test comparing the full model to one without the step.

Descriptive statistical analyses were performed using SPSS 16.0 for Windows<sup>®</sup> and multi-level models were built using MLWin 2.24<sup>®</sup>. All models were checked for multicollinearity (Tolerance <0.10). To correct for multiple testing we adjusted *p*-values using the False Discovery Rate method per model (i.e. the 3 baseline models, the models for change in period 1, the models for change in period 2 and the final model) (Benjamini, 1995). An adjusted *p*-value below 0.05 was considered statistically significant.

## RESULTS

### Patients

Between April 2008 and December 2010, 297 patients with a diagnosis of CFS and meeting all other inclusion criteria started CBT at our tertiary CFS specialist care centre. Ten patients dropped out from therapy before informed consent was asked and fifty-five refused to participate. The reason that was given most often for refusal was the perceived effort of having to do extra assessments during treatment. Of the 232 patients who gave informed consent, 217 completed the post treatment measurement (and 183 also completed at least two measurements during the study). A flowchart of the selection process is given in Fig. 1 and demographic characteristics of the study participants are given in Table 1. In total, 12 therapists participated in this study and they treated on average 18 patients (range 4–36).

### [FIGURE 1]

#### Factor analysis and internal consistency of Treatment Outcome Expectations Questionnaire

We performed an exploratory factor analysis with varimax rotation on the Treatment Outcome Expectations Questionnaire. This analysis indicated a two-factor structure. The first factor, named 'outcome expectations recovery', consisted of three questions: Treatment will help me to get rid of my symptoms; After treatment I will be less fatigued; After treatment I'll be recovered. Eigen-values were 0.87, 0.84 and 0.83 respectively and Cronbach's alpha was 0.83. The second factor, named 'outcome expectations coping', consisted of the questions: I'll learn to cope with my fatigue; I'll learn to accept my fatigue. Factor loadings were 0.67 and 0.87 respectively and Cronbach's alpha was 0.55. As we deemed this too low we used only the first factor for our analyses. Mean pre-treatment values are given in Table 1.

#### Predictive value of the baseline therapy relationship for post-treatment fatigue

For these analyses we selected the patients who had completed the post treatment measurement ( $n = 217$ ). In 20 patients some of the items or subscales of the assessment were not filled in. These values were replaced with the mean of the remaining items of the subscale or questionnaire. Baseline outcome expectations and working alliance are given in Table 1. Values indicate that outcome expectations and



working alliance were generally positive, as they lay in the upper half of the range of the questionnaires. Expectations of the therapists were extremely positive, as they expected a mean chance on recovery of 85%, which is considerably more than the actual percentage of patients that were no longer severely fatigued and impaired after therapy (68%, defined as a CIS fatigue <35 and Sip <700).

The null model showed that there was no variance at the therapist level (residual variance 0.00, s.e. 0.00), so we decided to proceed with single level models. Regression analyses (see Table 2) show that baseline patient characteristics explained 8% of variance in post-treatment fatigue ( $F = 3.0, p = 0.03$ ) and therapy relationship as rated by the patient added 25% of explained variance ( $F = 19.1, p = 0.001$ ). Expectations of recovery and task agreement proved a significant predictor of post treatment fatigue. Therapist-rated variables only added 3.5% of explained variance; the  $F$ -test indicated that their addition did not improve the model significantly ( $F = 2.8, p = 0.09$ ).

[TABLE 2]

**Predictive value of changes in the therapy relationship for post-treatment fatigue**

For the longitudinal analyses, we selected the 183 patients who had at least two interim measurements. We did not use the third interim measurement, as 67 patients did not complete the third interim measurement because the post-therapy measurement had already been planned or they dropped out. Changes in the first period (baseline to interim measurement 1) in patient rated therapy relationship, primarily outcome expectations, added 6% of explained variance ( $F$  change = 4.6;  $p = 0.004$ ) to the reduction of fatigue. Adding therapist ratings only led to an additional 3% of explained variance, which was not significant ( $F$  change 1.2;  $p = 0.39$ ). In the second period (interim measurement 1–2) similar results were seen. Changes in patient rated therapy relationship, again primarily outcome expectations, added 10% of explained variance in the reduction of fatigue ( $F$  change = 6.4;  $p = 0.001$ ), but adding therapist ratings only led to an additional 2% of explained variance, which was not statistically significant ( $F$  change 1.3;  $p = 0.35$ ) (Table 3a and Table 3b).

[TABLE 3A][TABLE 3B]

**The relative contribution of the therapy relationship and changes in fatigue perpetuating factors**

To assess the amount of variance in post-treatment fatigue explained by the therapy relationship and changes in fatigue-perpetuating factors, we built a model in which all factors that significantly predicted post-treatment fatigue in the previous models were added block-wise (i.e. first baseline characteristics, then therapy relationship at baseline, then changes in therapy relationship). The changes in fatigue-perpetuating factors were entered as a last step. This model explained 65% of post-treatment fatigue. A considerable proportion of variance was jointly explained by the therapy relationship and fatigue perpetuating factors (19%). The independent contribution of the therapy relationship at baseline was only 4% ( $F = 5.62; p = 0.002$ ), mostly attributable to therapist outcome expectations. Changes in the therapy relationship

during therapy did not explain any of the variance independently ( $F = 0.33$   $p = 0.67$  for the first period and  $F = 0.13$   $p = 0.72$  for the second). Changes in fatigue perpetuating factors independently explained 32% variance in post-treatment fatigue ( $F = 38.8$ ,  $p < 0.001$ ) (Table 4).

[TABLE 4]

## DISCUSSION

We studied, for the first time, the contribution of the therapy relationship to the reduction in fatigue during CBT for CFS in a large sample of patients and their therapists. Our study shows that especially patients' outcome expectations and task agreement at the start of treatment have a considerable influence on treatment outcome. They seem to exert their positive effect through a change in fatigue perpetuating factors.

### **Contribution of therapy relationship to the reduction in fatigue during CBT for CFS**

Outcome expectations and working alliance, especially patients' outcome expectations and agreement about what they should do in therapy, already explain 25% of the variance in post-treatment fatigue at the beginning of therapy. This is not due to a lower level of complaints, more somatic attributions or longer disease duration in patients with lower outcome expectations. Further changes in outcome expectations have a modest additional effect on the decrease in fatigue.

Contrary to our expectations, most patients with CFS have positive outcome expectations when starting CBT. Therapists generally expect a very positive outcome of CBT. White et al. found considerably lower outcome expectations of patients in their randomised controlled trial on CBT for CFS than in the present study (White et al., 2011). This may be because patients who participated in their trial could not choose which treatment they would start. Participants in our trial all accepted a referral for CBT and among those referred, they may have been those most motivated and confident about CBT.

From the three domains of working alliance that we measured, only task agreement predicted treatment outcome. This factor reflects the amount of agreement between patient and therapist about the content of therapy, i.e. what the patient has to do to achieve his or her goals. This factor is most likely related to the perceived credibility of the rationale of CBT for CFS. Only if patients support the cognitive behavioural model of CFS will they believe that changing cognitions and behaviour will help to reduce their fatigue. Goal agreement is an important element of our protocol and the patient is encouraged to define concrete therapy goals, often including getting back to work or hobbies, together with the therapist. Goal agreement was not related to therapy outcome, so it does not seem to be agreement about the goals of therapy per se, but rather agreement about how to reach these goals that predicts a good outcome. Patients may also have agreed about therapy goals while not expecting to reach them. The bond with the therapist did not predict treatment outcome. This may be due to the nature of the symptoms. Patients with somatic symptoms may have a more mechanical vision on therapy than patients with e.g. depression or anxiety. They may feel that the therapist is merely someone explaining the treatment and that the bond with the therapist therefore is less important.

Godfrey et al. (2007) studied the relationship between working alliance and treatment outcome in CBT for chronically fatigued patients of whom only a subset fulfilled criteria for CFS. They assessed roughly the same aspects of the working alliance as in the present study and named it working strategy consensus. This variable was also not related to treatment outcome. Other studies found a much larger effect of working alliance on treatment outcome of different psychotherapies (Gaston, Thompson, Gallagher, Cournoyer, & Gagnon, 1998; Horvath & Symonds, 1991). This may be related to the specific application of working alliance in CBT, in which collaborative empiricism has a large role (Dattilio & Hanna, 2012). Only two questions of the WAI ask about collaboration, so this concept may not be covered by this questionnaire (Tee & Kazantzis, 2011).

### **Relative contribution of therapy relationship and changes in fatigue-perpetuating factors**

Most of the positive effect of outcome expectations and working alliance on fatigue is shared with that of changes in fatigue perpetuating factors, so both seem to be part of the same process. A positive therapy relationship thus certainly seems to be beneficial, but not sufficient to decrease fatigue. Some concurrent change in fatigue perpetuating factors is also necessary. The other way around is also true: a change in fatigue perpetuating factors alone only partly explains the change in fatigue. This implies that outcome expectations and alliance play a crucial role in facilitating cognitive change.

A recent study on CBT for anxiety indeed indicates that a positive therapy relationship facilitates cognitive changes (Hoffart, Borge, Sexton, Clark, & Wampold, 2011), which then lead to a reduction in fatigue. A possible explanation for this finding could be that patients who have positive outcome expectations and who agree about the content of therapy are more engaged in therapy and are more compliant (Westra, Dozois, & Marcus, 2007). Alternatively, patients with positive outcome expectations may be more likely to expect that they can learn to control their fatigue, which is one of the fatigue perpetuating factors in CBT for CFS.

### **Limitations**

We assessed outcome expectations after the first session. Expectations may have already been influenced by the interventions of the therapist during the first session, e.g. by suggesting that recovery from CFS is possible. This may also explain the modest effect of changes during therapy. The advantage of measuring expectations after the first treatment session is that all patients have been properly informed and can base their expectations on reliable information. It would, however, be interesting to measure outcome expectations before and after the first session to determine changes in expectations brought on by the interaction with the therapist.

Outcome expectations were measured with questionnaires that have not previously been validated. The subscale 'recovery' of the Treatment Outcome Expectations Questionnaire showed good reliability. Therapists' outcome expectations were measured using a single Visual Analogue Scale, so reliability of this measurement may be low. Nevertheless, therapists' expectations of recovery were an important predictor of treatment outcome, independently of patients' expectations. We did not examine the predictive value of working alliance as seen by an independent assessor. Horvath et al. found that alliance best predicted treatment outcome when rated by the patient and least when rated by an independent observer (Horvath & Symonds,

1991). Martin, Garske, & Davis (2000) in a meta-analytic review, found however that the type of assessor (patient/therapist/independent) did not influence the relation between alliance and treatment outcome. This makes it unlikely that results from an independent assessor would have been entirely different.

Our study did not include a control group, however the fact that positive expectations at the start of the treatment are related to post treatment fatigue suggests a causal relationship. The fact that expectations no longer predicted post treatment fatigue when changes in fatigue-perpetuating factors were taken into account gives further support to the theory that positive expectations lead to a better treatment outcome through therapeutic processes and not because of other mechanisms unrelated to CBT.

Another limitation of our study is that patients who were less motivated for CBT and had less positive outcome expectations and working alliance may not have participated in our study. This may have led to a selection bias and may limit generalisability of our study results. However, assuming that we had a restricted range in outcome expectations and working alliance due to a selection bias makes it even more remarkable that we found an effect of outcome expectations in our sample. We did not measure patient participation within the session, but we measured patients' homework compliance. At the first measurement, 10% of the patients and 15% of the therapists stated that patients had never or only seldom done their homework, which increased to 11% and 25%, respectively, at the second interim measurement. This indicates that patients were relatively adherent. However, numbers were too low to compare treatment outcome between those adherent and non-adherent to therapy.

It is possible that working alliance was higher for those patients working with therapists who more competently used thought evaluation techniques. We did not directly measure therapists' competence or adherence to the protocol, but the multilevel analysis indicated almost no variation in treatment outcome between therapists. The same was found by Cella, Stahl, Reme, & Chalder, (2011). Wiborg, Knoop, Wensing, et al. (2012) did find differences in outcome between therapists. Their study was conducted in three secondary care centres in which CBT for CFS was being implemented. The centre in which therapists worked explained a part of the therapist effect. Both our study and that of Cella et al. were conducted in one highly specialised tertiary care centre, and all therapists participating in our study had been thoroughly trained in the protocol of CBT for CFS and received frequent intervision and supervision. This will probably have limited the differences between therapists and the way they performed CBT.

### **Implications for clinical practice and future research**

As the present study indicates that outcome expectations at the start of therapy may facilitate positive changes in fatigue-perpetuating factors, interventions aimed at establishing positive outcome expectations should be given as early in the intervention as possible to optimise their effect. Greenberg et al. suggested some approaches to optimise patients expectations that can also be applied to CBT for CFS (Greenberg, Constantino, & Bruce, 2006), such as installing a sense of hope, e.g. by changing illness representations of CFS that imply that someone has a chronic illness that is unchangeable into an illness that can be positively influenced by the patient. Extensively explaining the underlying rationale of CBT and explicitly asking for the

opinion of the patient and significant others to the rationale may help to improve outcome expectations.

Although some authors suggest otherwise (Van Houdenhove, 2006), our results that expectations of recovery are associated with therapy outcome suggest it is important that therapists discuss the possibility of a full recovery (Knoop et al., 2007). They can make the concept of recovery more tangible by letting the patient define what he or she would like to do when he/she did not have CFS anymore and translate this into concrete therapy goals.

### **CONCLUSIONS**

Expectations of recovery and agreement about the content of treatment contribute to actual treatment outcome. This study enhances the understanding of the process of change during CBT for CFS as it shows that these factors do not have a direct positive effect on post-treatment fatigue, but seem to facilitate cognitive changes during CBT for CFS.

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### **CONFLICT OF INTEREST**

No interests to declare.

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### **APPENDIX A. SUPPLEMENTARY DATA**

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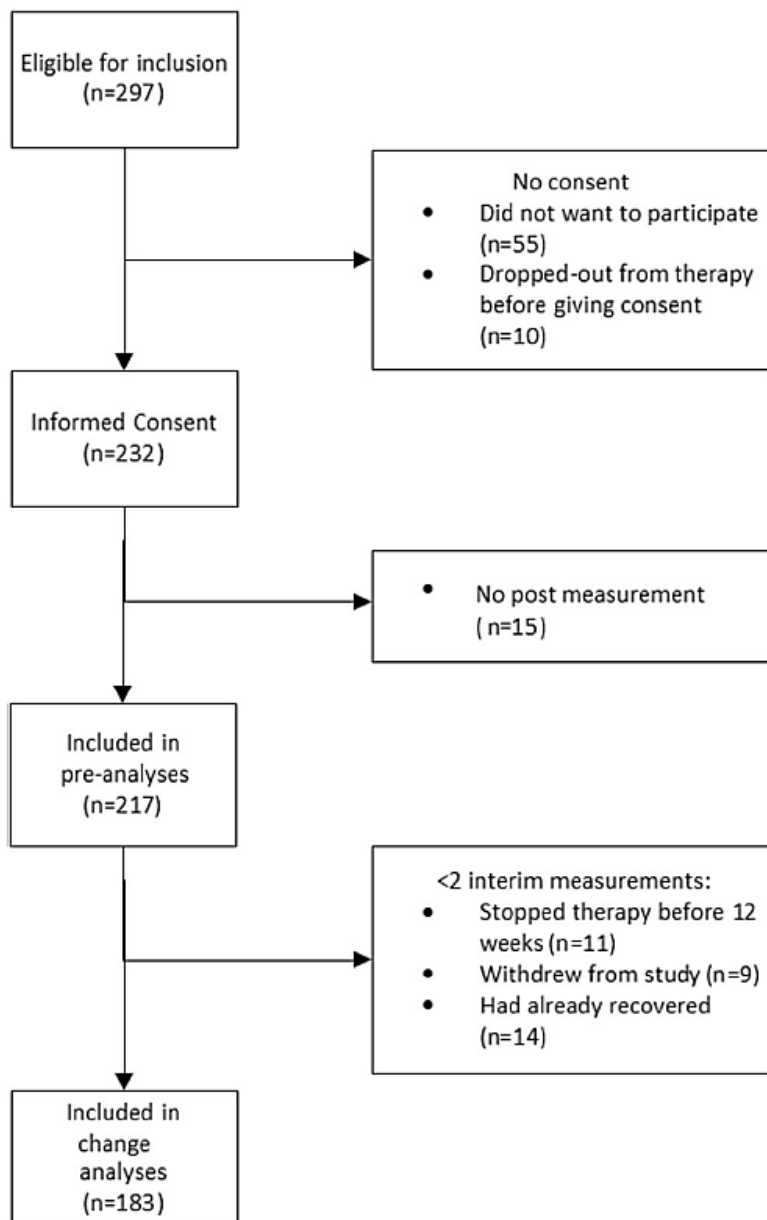
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## APPENDIX, FIGURES AND TABLES

Fig. 1. Flow chart of the selection of the study participants



**Table 1**  
Baseline characteristics ( $n = 217$ ).

Variable	Mean (sd)
Age (years)	37.8 (11.2)
Female	162 (74.7%)
CIS fatigue	49.7 (5.4)
SIP total score	1535 (560)
No. CDC symptoms	7 (1.7)
Symptom durations (years)	5.0 (3.0–10.8)
<b>Patient</b>	
WAI-s Task	16.2 (2.5)
WAI-s Bond	15.1 (2.4)
WAI-s Goal	16.7 (2.4)
Expectations	10.2 (1.4)
<b>Therapist</b>	
WAI-s Task	16.5 (2.0)
WAI-s Bond	16.4 (1.8)
WAI-s Goal	16.4 (2.2)
Expectations	85 (73–93)

\* Absolute number (percentage) are given. CIS fatigue = Checklist Individual strength; Outcome expectations = Therapy Outcome Expectations Questionnaire; SIP = Sickness Impact Profile; WAI-S=Working Alliance Inventory Short Form.

**Table 2**  
Prediction models of baseline patient and therapist rated therapy relationship ( $n = 217$ ).

	1			2			3		
	B(se)	t	p	B(se)	t	p	B(se)	t	p
Baseline									
Fatigue pre	0.44(0.18)	2.45	0.06	<b>0.51(0.16)</b>	<b>3.20</b>	<b>0.01</b>	<b>0.48(0.16)</b>	<b>3.00</b>	<b>0.02</b>
Sex	3.57(2.28)	1.57	0.21	0.78(1.99)	0.39	0.73	-0.03(1.98)	-0.01	0.99
Age (year)	0.14(0.09)	1.50	0.22	0.17(0.08)	2.11	0.10	0.14(0.08)	1.82	0.16
Phys attr	0.20(0.35)	0.57	0.63	-0.37(0.31)	-1.21	0.33	-0.41(0.30)	-1.34	0.28
SIP pre	0.00(0.00)	1.18	0.33	0.00(0.00)	1.70	0.18	0.00(0.00)	1.84	0.17
Duration (mth)	0.14(0.09)	1.57	0.21	0.11(0.08)	1.33	0.28	0.07(0.08)	0.93	0.47
<b>Patient</b>									
WAI-s Task				<b>-1.40(0.50)</b>	<b>-2.80</b>	<b>0.03</b>	<b>-1.40(0.50)</b>	<b>-2.79</b>	<b>0.03</b>
WAI-s Bond				0.10(0.42)	0.24	0.83	0.24(0.42)	0.57	0.63
WAI-s Goal				0.47(0.54)	0.87	0.48	0.40(0.54)	0.75	0.53
Expectations				<b>-4.28(0.67)</b>	<b>-6.39</b>	<b>&lt;0.001</b>	<b>-3.96(0.69)</b>	<b>-5.75</b>	<b>&lt;0.001</b>
<b>Therapist</b>									
WAI-s Task							1.24 (0.67)	1.87	0.15
WAI-s Bond							-0.47(0.58)	-0.80	0.52
WAI-s Goal							-0.73 (0.56)	-1.31	0.28
Expectations							<b>-0.16(0.060)</b>	<b>-2.52</b>	<b>0.03</b>
(Constant)	-7.47(10.36)	-0.72		52.59 (11.57)	4.55		63.04(12.54)	5.03	
R <sup>2a</sup>	0.078		0.03	0.330		<0.001	0.365		0.09

Dependent Variable: Checklist Individual Strength subscale fatigue post therapy. Fatigue = Checklist Individual strength; Expectations = Therapy Outcome Expectations Questionnaire; Phys attr = Causal attribution list subscale physical attributions; SIP = Sickness impact profile; WAI-S=Working Alliance Inventory Short Form. Bold indicates  $p < 0.05$ .

<sup>a</sup> R<sup>2</sup> and t-value for F-test of change.

**Table 3a**  
Prediction models of change in patient and therapist rated therapy relationship early in therapy ( $n = 183$ ).

	1			2			3		
	B(se)	t	p	B(se)	t	p	B(se)	t	p
<i>Baseline</i>									
Fatigue pre	<b>0.46(-0.16)</b>	<b>2.80</b>	<b>0.02</b>	<b>0.41(0.16)</b>	<b>2.56</b>	<b>0.04</b>	<b>0.36(0.16)</b>	<b>2.21</b>	<b>0.08</b>
WAI-s Task pt	-1.17(0.52)	-2.25	0.08	-0.62(0.68)	-0.92	0.54	-0.81(0.68)	-1.19	0.44
WAI-s Bond pt	0.07(0.44)	0.17	0.91	-0.36(0.50)	-0.72	0.63	-0.30(0.50)	-0.61	0.68
WAI-s Goal pt	0.35(0.56)	0.62	0.68	0.79(0.81)	0.97	0.54	0.95(0.82)	1.17	0.43
Expectations pt	<b>-3.32(0.71)</b>	<b>-4.70</b>	<b>&lt;0.001</b>	<b>-4.60(0.80)</b>	<b>-5.73</b>	<b>&lt;0.001</b>	<b>-4.24(0.84)</b>	<b>-5.07</b>	<b>&lt;0.001</b>
WAI-s Task ther	1.37(0.70)	1.95	0.12	1.46(0.68)	2.14	0.08	0.24(0.97)	0.25	0.87
WAI-s Bond ther	-0.45(0.62)	-0.73	0.63	-0.51(0.60)	-0.86	0.56	-0.41(0.79)	-0.52	0.67
WAI-s Goal ther	-0.75(0.60)	-1.24	0.42	-0.85(0.60)	-1.43	0.32	0.06(0.82)	0.08	0.96
Expectations ther	<b>-0.24(0.06)</b>	<b>-3.79</b>	<b>&lt;0.001</b>	<b>-0.24(0.06)</b>	<b>-3.86</b>	<b>&lt;0.001</b>	<b>-0.23(0.07)</b>	<b>-3.45</b>	<b>0.004</b>
<i>Patient</i>									
Δ WAI-s Task				0.40(0.57)	0.71	0.63	0.33(0.57)	0.58	0.68
Δ WAI-s Bond				-0.78(0.45)	-1.73	0.21	-0.70(0.46)	-1.52	0.29
Δ WAI-s Goal				0.35(0.71)	0.49	0.70	0.39(0.72)	0.55	0.68
Δ Expectations				<b>-3.02(0.83)</b>	<b>-3.65</b>	<b>&lt;0.001</b>	<b>-2.92(0.84)</b>	<b>-3.48</b>	<b>0.004</b>
<i>Therapist</i>									
Δ WAI-s Task							-1.63(0.83)	-1.96	0.12
Δ WAI-s Bond							0.01(0.79)	0.02	0.99
Δ WAI-s Goal							0.93(0.70)	1.32	0.38
Δ Expectations							0.05(0.05)	0.91	0.54
constant	67.08(11.99)	5.60		74.39(11.81)	6.30		75.46(12.44)	6.07	
R <sup>2</sup>	0.323		<0.001	0.386		0.004	0.403		0.47

Dependent Variable: Checklist Individual Strength subscale fatigue post therapy. Fatigue = Checklist Individual strength; Expectations = Therapy Outcome Expectations Questionnaire; WAI-S=Working Alliance Inventory Short Form.  
R<sup>2</sup> and t-value for F-test of change. Bold indicates  $p < 0.05$ .

**Table 3b**  
Prediction models of change in patient and therapist rated therapy relationship mid-therapy ( $n = 183$ ).

	1			2			3		
	B(se)	t	p	B(se)	t	p	B(se)	t	p
<i>Baseline</i>									
Fatigue pre	0.23 (0.19)	1.23	0.39	0.12 (0.18)	0.68	0.57	0.14(0.19)	0.74	0.57
WAI-s Task pt int1	-0.65 (0.56)	-1.16	0.40	-0.85 (0.72)	-1.18	0.40	-0.93(0.73)	-1.28	0.39
WAI-s Bond pt int1	-0.41(0.44)	-0.94	0.51	0.01(0.48)	0.02	0.98	-0.20(0.49)	-0.41	0.77
WAI-s Goal pt int1	0.79(0.76)	1.04	0.45	0.52(0.93)	0.56	0.68	0.65(0.94)	0.69	0.59
Expectations pt int1	<b>-3.35(0.78)</b>	<b>-4.31</b>	<b>0.001</b>	<b>-3.65(0.87)</b>	<b>-4.22</b>	<b>0.001</b>	<b>-3.02(0.91)</b>	<b>-3.31</b>	<b>0.008</b>
WAI-s Task ther int1	-1.67(0.91)	-1.84	0.25	-1.78(0.86)	-2.06	0.19	-2.16(1.14)	-1.89	0.23
WAI-s Bond ther int1	-0.12(0.78)	-0.15	0.95	0.04(0.73)	0.05	0.98	0.77(0.86)	0.91	0.51
WAI-s Goal ther int1	1.35(0.78)	1.74	0.26	1.14(0.73)	1.56	0.32	1.25(1.00)	1.25	0.38
Expectations ther int1	-0.06(0.05)	-1.22	0.39	-0.07(0.05)	-1.41	0.35	-0.20(0.08)	-2.49	0.06
<i>Patient</i>									
Δ WAI-s Task				-1.29(0.67)	-1.91	0.23	-1.10(0.67)	-1.64	0.30
Δ WAI-s Bond				0.77(0.51)	1.50	0.34	0.66(0.51)	1.31	0.38
Δ WAI-s Goal				-0.58(0.66)	-0.88	0.51	-0.59(0.67)	-0.87	0.51
Δ Expectations				-2.01(0.74)	-2.71	0.06	-1.27(0.81)	-1.57	0.32
<i>Therapist</i>									
Δ WAI-s Task							-0.17(0.90)	-0.19	0.94
Δ WAI-s Bond							0.93(0.86)	1.08	0.44
Δ WAI-s Goal							-0.11(0.82)	-0.13	0.95
Δ Expectations							-0.18(0.09)	-2.08	0.19
constant	65.41 (13.98)	4.68		77.69(13.77)	5.64		76.42(14.35)	5.33	
R <sup>2</sup>	0.277		0.001	0.380		0.001	0.340		0.35

Dependent Variable: Checklist Individual Strength subscale fatigue post therapy. Fatigue = Checklist Individual strength; Expectations = Therapy Outcome Expectations Questionnaire; WAI-S=Working Alliance Inventory Short Form.  
R<sup>2</sup> and t-value for F-test of change. Bold indicates  $p < 0.05$ .

**Table 4**  
Final model of specific and non-specific factors ( $n = 183$ ).

	B(se)	<i>t</i>	<i>p</i>
Fatigue pre	0.88(0.13)	6.96	<0.001
Task pt pre	-0.54(0.28)	-1.91	0.09
Expect pt pre	-0.70(0.63)	-1.11	0.38
Expect ther pre	-0.11(0.04)	-2.71	0.02
Δ Expect pt 1	-0.38(0.66)	-0.57	0.69
Δ Expect pt 2	-0.18(0.51)	-0.36	0.77
Δ Focus	0.15(0.08)	1.96	0.09
Δ Control	-0.82(0.17)	-4.76	<0.001
Δ Perc activity	0.55(0.14)	3.97	<0.001
Δ Phys funct	-0.19(0.04)	-5.02	<0.001
Constant			

Dependent Variable: Checklist Individual Strength subscale fatigue post therapy. Control = Self-efficacy Scale; Fatigue = Checklist Individual strength; Expectations = Therapy Outcome Expectations Questionnaire; Focus = Illness Management Questionnaire subscale focusing on symptoms; Perc activity = Checklist Individual Strength subscale physical activity; Phys funct = MOS SF-36 subscale physical functioning WAI-S=Working Alliance Inventory Short Form. Bold indicates  $p < 0.05$ .