Moderators of the treatment response to guided self-instruction for chronic fatigue syndrome

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ABSTRACT

Objective: The efficiency and efficacy of guided self-instruction for chronic fatigue syndrome (CFS) can be enhanced if it is known which patients will benefit from the intervention. This study aimed to identify moderators of treatment response.

Methods: This study is a secondary analysis of two randomized controlled trials evaluating the efficacy of guided self-instruction for CFS. A sample of 261 patients fulfilling US Center for Disease Control and Prevention criteria for CFS was randomly allocated to guided self-instruction or a wait list. The following potential treatment moderators were selected from the literature: age, fatigue severity, level of physical functioning, pain, level of depressive symptoms, self-efficacy with respect to fatigue, somatic attributions, avoidance of activity, and focus on bodily symptoms. Logistic and linear regression analyses were used with interaction term between treatment response and the potential moderator.

Results: Age, level of depression, and avoidance of activity moderated the response to guided self-instruction. Patients who were young, had low levels of depressive symptoms, and who had a low tendency to avoid activity benefited more from the intervention than older patients and patients with high levels of depressive symptoms and a strong tendency to avoid activity.

Conclusion: Guided self-instruction is exclusively aimed at cognitions and behaviours that perpetuate fatigue. Patients with severe depressive symptom may need more specific interventions aimed at the reduction of depressive symptoms to profit from the intervention. Therefore we suggest that patients with substantial depressive symptoms be directly referred to regular cognitive behaviour therapy.

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Introduction

Chronic fatigue syndrome (CFS) is characterized by medically unexplained, prolonged and disabling fatigue. According to the widely used consensus criteria of the US Center for Disease Control, there have to be at least four of the following eight additional symptoms present for the CFS diagnoses to be warranted: sleep that does not alleviate fatigue, post-exertion malaise, headaches, muscle pain, multi-joint pain, sore throat, tender lymph nodes, and impaired concentration or memory [1]. Cognitive behaviour therapy (CBT) is directed at changing cognitions and behaviours that perpetuate fatigue [2] and has been shown to be effective in reducing fatigue and disabilities in patients with CFS [3,4]. However, CBT for CFS is only effective after 13–16 sessions [5–8]. As not all patients need such intensive treatment, a self-guided intervention has been developed [9], based on the protocol of CBT for CFS. Instead of face-to-face sessions, patients go through a self-help booklet with assignments, at their own pace and with email guidance from a therapist.

Two randomized controlled trials (RCTs) evaluated the effectiveness of guided self-instruction for CFS compared to patients with CFS on a wait list [9,10]. The first RCT was performed in a tertiary treatment centre. Cognitive behavioural therapists who had extensive experience in treating patients with CBT for CFS carried out the intervention [9]. In the second RCT, psychiatric nurses in a community-based mental health-care centre (MHC) were trained to deliver the guided self-instruction. Before the start of the study the psychiatric nurses were unacquainted with CBT and the treatment of CFS [10]. In both trials patients who followed the minimal intervention reported a significant reduction in fatigue [9,10]. However, the minimal intervention sufficed for only a subgroup of the patients. Patients who did not profit from the minimal intervention were referred to additional CBT. It has been shown that patients can profit from additional CBT if the minimal intervention is unsuccessful [11].

Stepped care for CFS, consisting of guided self-instruction and followed by additional CBT if needed, offers the opportunity to make the treatment of CFS more efficient. Efficiency can be further enhanced if patients who are likely to profit from the minimal

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intervention can be identified. Identifying moderators is a way to understand the variability of outcomes in psychosocial interventions. Knowing moderators of guided self-instruction will inform which patients are likely to benefit from the intervention. It has already been shown that patients with an extremely high level of disabilities profit less from the minimal intervention compared to those without severe disabilities [9]. These patients may have better treatment outcomes with regular CBT than with the minimal intervention.

Studies that investigated moderators and predictors of treatment outcome in face-to-face CBT for CFS were reviewed. These studies show that focusing on bodily symptoms and attributing symptoms to a physical cause are related to poor treatment outcomes [12,13]. However, evidence concerning the latter is contradictory [6,13,14]. Additionally, patients with a high sense of control with respect to fatigue gain greater benefit from CBT than those with a low sense of control [6] and patients with a low activity pattern tend to show less improvement following CBT compared to those with a high activity pattern [6]. After adapting the treatment manual of CBT for CFS, the relation between the level of physical activity and treatment outcome was no longer present [15]. Good CBT treatment outcomes are associated with a change in avoidance of activity and related beliefs [16]. The prognostic role of depression is still unclear. Some studies found that depression was negatively related to treatment outcomes, whereas others found no relation [17–19]. A recently published study found that baseline levels of depressive symptoms, measured with the HADS, significantly moderated fatigue at 1-year follow-up in an behavioural minimal intervention for CFS [20]. In contrast with these findings Prins et al. [18] found that patients with depression and psychological distress benefited from CBT as much as others. There is also evidence to suggest that high levels of pain are negatively correlated with treatment outcome [21]. In addition, treatment seems to be less successful when patients are older, are members of a self-help group, are involved in a legal procedure concerning disability related benefits, or received a disablement insurance benefit [6,7,17].

This study investigated whether factors that are related to treatment outcome in CBT, are moderators of response to guided self-instruction on fatigue. Most studies use the continuous post-treatment score in fatigue as a dependent variable to gain insight in predictors or moderators of treatment outcome instead of significant clinical improvement in fatigue. However, the latter is clinically more meaningful. Therefore, in *post-hoc* analyses we aimed to identify moderators of post-treatment fatigue (continuous) and significant clinical improvement in fatigue (dichotomous) following guided self-instruction. Analysis were adjusted for baseline levels of fatigue.

Method

This study is a secondary analysis of data obtained in two RCTs (NTR570 and NTR1223) that tested the effectiveness of guided self-instruction for CFS compared with people with CFS who were on a wait list. Patients doing the guided self-instruction went through a booklet with assignments. They did this at their own pace, and they had email contact with a therapist. Patients on the wait list received CBT or the minimal intervention after a delay of six months. Both trials showed that after guided self-instruction significantly more patients reported a significant clinical improvement in fatigue. Patients were regarded significantly clinically improved with respect to fatigue if (1) the change in fatigue was statistically reliable (reliable change index > 1.96) [22] and (2) the fatigue score at post-treatment was <35 on the Checklist Individual Strength (CIS) subscale fatigue severity [23]. The other main findings of both RCTs are published elsewhere [9,10]. To explore moderators of treatment outcomes of guided self-instruction, we re-analysed data from the two RCTs. After baseline assessment, patients were randomly assigned to either the minimal intervention or a wait list. Assessment took place prior and subsequent to treatment or placement on a wait list.

Samples

Participants were 261 patients meeting Center for Disease Control (CDC) criteria for CFS [1]. The ethic committee of the Radboud University Nijmegen Medical Centre approved of both studies, and written informed consent was obtained from all patients. The first RCT tested the efficacy of guided self-instruction in a tertiary treatment centre [9]. Patients were 18 years or older and able to speak and read Dutch. A medical and psychiatric evaluation was performed to exclude other causes of fatigue. All patients were severely fatigued (CIS, subscale fatigue severity ≥ 35), and severely disabled (Sickness Impact Profile (SIP), total score ≥ 700) [23,24]. In total 169 patients were randomly assigned to either guided self-instruction or a wait list. During guided self-instruction, qualified cognitive behavioural therapists gave patients feedback on their assignments. In total ten patients (guided self-instruction n = 6, wait list n = 4) did not complete second assessment. Complete data were available for 78 patients following the intervention, and for 81 patients after the wait period.

The second RCT was delivered by psychiatric nurses in a community-based MHC [10]. All patients, aged between 18 and 65, were severely fatigued (CIS, subscale fatigue severity ≥ 35) for at least six months and reported physical and/or social disabilities in daily functioning (Medical Outcomes Survey Short Form-36 (SF-36), subscale physical and/or social functioning ≤ 70) [23,25]. Initially, 123 patients were randomly assigned, to either guided self-instruction (n = 62) or a wait list (n = 61). Seven patients following guided self-instruction and five patients of the waiting list did want to complete second assessment. Twelve patients (six patients of the intervention condition and six patients of the wait list) were excluded from analysis because of medical or psychiatric co-morbidity that could explain the fatigue. Misclassifications were confirmed by the nurse in attendance. Seven of the patients receiving a wrong diagnosis, did not also complete the second assessment. As a result, 52 patients included in the intervention had a complete assessment, and 50 patients after the wait period.

Design

Based on the existing literature of moderators and predictors of treatment outcome of CBT for CFS, the following variables were selected; age, fatigue severity, level of physical functioning, impact of pain, level of depressive symptoms, self-efficacy with respect to fatigue, somatic attributions, avoidance of activity, and focus on bodily symptoms. Information on participants being members of a self-help group, if they were involved in a legal procedure concerning disability related benefits, or if they had received disablement insurance was unavailable.

Assessments

Sociodemographic characteristics
Gender, age, level of education, and civil status of participants were noted.

CFS symptoms

Fatigue. The subscale fatigue severity of the CIS was used to measure the experienced fatigue over the past two-week period prior to testing [23]. This subscale consists of eight items, each scored on a 7-point Likert scale. High scores indicate a high level of fatigue. A commonly used cut-off score for fatigue severity is 35 (or higher). This score is two standard deviations above the mean of healthy