



## Does neuropsychological test performance predict outcome of cognitive behavior therapy for Chronic Fatigue Syndrome and what is the role of underperformance? ☆

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### ABSTRACT

**Objective:** A subgroup of patients with Chronic Fatigue Syndrome (CFS) has cognitive impairments, reflected by deviant neuropsychological test performance. However, abnormal test scores can also be caused by suboptimal effort. We hypothesized that worse neuropsychological test performance and underperformance were related to each other and to a smaller reduction in fatigue, functional impairments, physical limitations and higher drop-out rates following cognitive behavior therapy (CBT) for CFS.

**Methods:** Data were drawn from a previous trial, in which CFS patients were randomized to two conditions; 1) guided self-instruction and additional CBT (n = 84) or 2) waiting period followed by regular CBT for CFS (n = 85). Underperformance was assessed using the Amsterdam Short Term Memory Test (<84). To test neuropsychological test performance, the Symbol Digit Modalities Task, a simple reaction time task and a choice reaction time task were used. Interaction effects were determined between underperformance and neuropsychological test performance on therapy outcomes.

**Results:** Underperformance was associated to worse neuropsychological test performance, but there were no significant interaction effects of these two factors by therapy on fatigue severity, functional impairments and physical limitations, but there was a significant main effect of underperformance on functional impairments, physical limitations and dropout rates.

**Conclusion:** Underperformance or neuropsychological test performance was not related to the change in fatigue, functional impairments, and physical limitations following CBT for CFS. However, underperforming patients did drop out more often. Therapists should pay attention to beliefs and behavioral or environmental factors that might maintain underperformance and increase the risk of dropout.

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### Introduction

Chronic Fatigue Syndrome (CFS) is characterized by somatically unexplained severe fatigue, lasting longer than six months and leading to substantially impaired functioning. According to the U.S. Center for Disease Control (CDC) criteria for CFS, four out of eight accompanying

symptoms must be present: muscle pain, multi-joint pain, headaches, sore throat, tender lymph nodes, unrefreshing sleep, post-exertional malaise, and concentration and memory problems [1,2].

The majority of CFS patients report cognitive disabilities. However, only a subgroup of CFS patients shows signs of objective impairment when cognitive functioning is assessed with neuropsychological tests. For example, a study by Vercoelen et al. (1998) showed that the majority of patients reported concentration and memory problems (respectively 74% and 69%), while only a minority (27%) had deviant scores on neuropsychological tests [3]. This disparity between the prevalence of subjective and objectively assessed cognitive impairments is often found [3–5].

The exact prevalence and nature of objective cognitive impairments in CFS patients is not clear, as this depends on the methodological approaches, participant selection criteria and statistical analyses. The most consistent findings regarding cognitive impairments in CFS are slower information processing and impaired attention and memory [3,6–9].

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It is difficult to distinguish whether impaired test results are due to underperformance or cognitive impairment. Neuropsychological tasks require effort and when a patient's effort is suboptimal, the test results are difficult to interpret [10]. However, possible suboptimal test effort is seldom the focus of study in CFS patients. Two studies found that about a quarter of CFS patients obtained scores indicative of underperformance, which was substantially higher than in patients with a known neurological disease [11,12]. However, other studies that tested underperformance in samples of CFS patients found low levels of reduced effort [13] or suboptimal effort was even absent [14]. Furthermore, studies comparing the prevalence of suboptimal effort of CFS patients with that of healthy controls showed inconsistent results. Some studies did find differences between the two groups [15], while others did not [13,16]. Inconsistent findings could be explained by the fact that various instruments were used to assess suboptimal effort. Although we do not exactly know how common underperformance is among CFS patients, we expect that patients who show underperformance or have worse neuropsychological test performance are in part overlapping groups, but this needs to be confirmed.

Patients who perform below normal expectations can do this intentionally or unintentionally and therefore various terms are used in literature, such as suboptimal performance or effort, underperformance, poor motivation, and for intentional behavior malingering, or feigning. Various explanations for the tendency of CFS patients to underperform have been put forward. CFS patients who complain about memory and concentration deficits might experience excessive stress when confronted with a memory task or assume beforehand that they will fail on such a task. Alternatively, CFS patients might fear that their problems go unnoticed on a relatively easy task and adjust their efforts to their disease expectations. The unknown etiology of CFS and subsequent fear of complaints not being taken seriously could enhance the tendency to underperform [11]. It has been demonstrated that patients' body consciousness was related to information processing speed [12]. This suggests that cognitive processes that play a role in maintaining fatigue, such as a focus on bodily symptoms, also play a role in the reduced neuropsychological test performance.

Cognitive behavior therapy (CBT) for CFS proved to be an effective treatment. Various randomized controlled trials (RCTs) have demonstrated that CBT for CFS leads to a significant decrease in fatigue and disabilities [17]. However, not all CFS patients benefit equally from therapy [18]. One might expect that CFS patients with cognitive impairments or showing underperformance might benefit less from CBT for CFS. Patients with cognitive impairment might benefit less from therapy, because verbal therapy requires various mental processes, such as attention, reasoning, planning, and decision making. To explain why underperforming CFS patients benefit less from therapy we need to look at the underlying reason for underperformance. When a patient underperforms to ensure that the consequences of the condition will be noticed or because a patient is focused on symptoms, he/she might benefit less from CBT because this therapy motivates patients to reduce the focus on symptoms by diverting attention away from fatigue and not to discuss symptoms with others. Distress related to failing on tasks might not only explain underperformance on memory tasks, but also generalize to other situations. Therefore one might expect that patients who show underperformance might drop out of therapy more often. To summarize, we expect that worse neuropsychological test performance and underperformance have a negative impact on outcome of CBT for CFS, but to our knowledge this hypothesis has not been investigated before.

Therefore we had the following research questions. First, we tested whether underperformance was related to worse neuropsychological test performance. Second, we tested whether CFS patients who showed underperformance or worse neuropsychological test performance benefitted less from CBT for CFS. We hypothesized that underperformance and worse neuropsychological test performance were related to a smaller reduction in fatigue functional impairments, physical limitations and higher dropout rates.

## Method

### Patients and procedure

Data for the current study were drawn from a previously published randomized non-inferiority trial in which stepped care for CFS was compared to care as usual [19]. The current study consisted of a controlled and a non-controlled intervention studies. The first part was a RCT in which guided self-instruction was compared to waiting list. The second part was a non-controlled follow-up study in which patients who received stepped care for CFS (guided self-instruction followed by additional CBT) were combined with patients who received care as usual (regular CBT for CFS after a waiting period). Because the non-inferiority trial demonstrated that stepped care for CFS was just as effective as care as usual it seemed justified to combine stepped care with care as usual.

Between February 2006 and September 2007 CFS patients were recruited for the study. Eligibility criteria were: meeting the criteria for CFS according to the U.S. Center for Disease Control [1,2]; being 18 years or older; being able to speak and read Dutch, and not being involved in a legal procedure concerning disability-related financial benefits.

CFS patients were referred for CBT to the Expert Centre for Chronic Fatigue of the Radboud University Nijmegen Medical Centre. After referral patients completed the baseline assessment (T0) and were placed on a waiting period for CBT for CFS, because of limited treatment capacity. Patients on the waiting period were offered to participate in a randomized controlled trial testing the efficacy of guided self-instruction. Patients who agreed to participate provided written informed consent and subsequently were assigned to one of two conditions; guided self-instruction or waiting for CBT for CFS. After guided self-instruction or waiting for CBT patients were assessed again (T1). Thereafter all patients were offered CBT; additional CBT after guided self-instruction and regular CBT for CFS for patients after the waiting period. Patients were assessed for a third time (T2) after stepped care or care as usual for CFS.

### Interventions

The guided self-instruction intervention consisted of a booklet and therapist support by e-mail. The booklet was based on the protocol of CBT for CFS [20] and contained information about CFS and weekly assignments. Patients were invited to send their therapist an e-mail (or call their therapist if they did not e-mail) at least once every two weeks to report on their progress and ask questions about the self-instruction. The program took at least 16 weeks. The intervention is described in detail elsewhere [19,21].

Regular CBT for CFS was provided according to a published protocol [20]. The protocol is based on the model of fatigue perpetuating factors [22]. The aim of the 'face-to-face' therapy is to reduce fatigue and disabilities by changing fatigue-related cognitions and behaviors. CBT for CFS consists of about 14 sessions during a 6 month period.

### Instruments

*Education* was assessed by self-report from primary school to university and divided into 7 levels. The latter two levels were categorized as being highly educated (higher vocational education or university).

Two tests were used to investigate *neuropsychological test performance*. The first test was a *reaction time task*. The reaction time task measures the speed of information processing and is comprised of two consecutive tasks, a simple- and a choice-reaction time task, resulting in two reaction times (simple RT and choice RT). On a response board, five target buttons are situated in an arch around a start button. The target buttons are placed at equal distances from the start button. Each target button contains a stimulus light. In both tasks, the participant keeps

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