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BRIEF CLINICAL REPORT

Internet-delivered cognitive behavioural therapy for chronic fatigue among adolescents with a chronic medical condition: a single case study

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Abstract

Background: Severe fatigue is a prominent symptom among adolescents with a chronic medical condition, with major impact on their well-being and daily functioning. Internet-based cognitive behavioural therapy (I-CBT) is a promising treatment for severe fatigue among adolescents with a chronic medical condition, but its effectiveness has not been studied.
Aims: We developed an I-CBT intervention for disabling fatigue in a chronic medical condition and tested its feasibility and effectiveness in an adolescent with an immune dysregulation disorder (IDD), namely juvenile idiopathic arthritis (JIA).
Method: The application of I-CBT is illustrated through a clinical case study of a 15-year-old girl with JIA and chronic severe fatigue. An A-B single case experimental design was used with randomization of the waiting period prior to start of the intervention. Outcomes were weekly measures of fatigue severity, physical functioning, school absence and pain severity.
Results: Fatigue severity significantly decreased following I-CBT. Improvements were observed towards increased school attendance and improved physical functioning following the intervention, but these effects were too small to become significant.
Conclusions: The study provides preliminary support for the feasibility and effectiveness of the application of I-CBT for severe fatigue in adolescents with a long-term medical condition.

Keywords: adolescent; chronic disease; chronic medical condition; cognitive behaviour therapy; disease activity; fatigue; juvenile idiopathic arthritis

Introduction

Severe fatigue is frequently reported by adolescents and when persistent it leads to significant physical and social impairments (Rimes *et al.*, 2007). Internet-delivered cognitive behaviour therapy (I-CBT) is an evidence-based treatment for myalgic encephalitis/chronic fatigue syndrome (ME/CFS) (Albers *et al.*, 2021). According to the model applied in CBT for ME/CFS, the trigger of severe fatigue should be discerned from fatigue-related behaviours and beliefs which perpetuate the fatigue (Goërtz *et al.*, 2021). CBT focuses on these dysfunctional beliefs and behaviours.

Adolescents with an immune dysregulation disease (IDD) are prone to severe fatigue (Nijhof *et al.*, 2021). IDD includes a myriad of immunological disorders, such as juvenile idiopathic arthritis, auto-inflammatory disorders and primary immunodeficiencies. Severe fatigue in adolescents with IDD is associated with lower health-related quality of life, a high prevalence of reported pain, and limitations in daily activities (Nijhof *et al.*, 2021). The relationship between fatigue and disease-specific biological causes in IDD is absent or weak, while pain and fatigue are strongly associated (Nijhof *et al.*, 2021). As observed in ME/CFS, beliefs and behavioural factors are involved in the perpetuation of fatigue in IDD. Likewise, addressing these factors is the starting point for appropriate therapeutic interventions.

The cognitive behavioural model of chronic fatigue in medical conditions assumes that disease-specific factors trigger fatigue, whereas cognitive behavioural factors can perpetuate fatigue. CBT aimed at reducing fatigue is efficacious in adult patients with a medical condition (Goërtz *et al.*, 2021). Fatigue in paediatric medical conditions is associated with generic transdiagnostic, psychological and social factors, which are promising avenues for CBT (Nap-van der Vlist *et al.*, 2021). We therefore hypothesized that severely fatigued adolescents with a chronic medical condition may benefit from CBT targeting of these perpetuating factors.

A novel I-CBT for chronically fatigued adolescents (*FITNET-plus*) was tested and applied in an adolescent with juvenile idiopathic arthritis (JIA), a major IDD. The aim of this study was to gain insight in (a) the feasibility of treating severe fatigue with I-CBT in a paediatric patient diagnosed with IDD and (b) the effectiveness of I-CBT in reducing fatigue directly after treatment and at longer term follow-up.

A single case experimental design (SCED) was conducted, including a randomized time interval prior to the start of the intervention and using time series to evaluate the feasibility and effectiveness following I-CBT. This single case study was part of a larger study with nine patients with an IDD. In this paper, one case is described in depth to enable a thorough introduction of this novel treatment. Furthermore, in an explorative analysis, patient experiences and the effect of I-CBT on fatigue severity, pain severity and limitations in daily functioning was determined.

Method

Case presentation

Sarah (pseudonym) was known to have both arthralgia and severe fatigue since the age of 14. No medical diagnosis could be made at that time, and supportive care was offered. At age 15, arthritis appeared and JIA was diagnosed. She was treated with a TNF alpha blocking agent (Humira) and Methotrexate (MTX), leading to disease remission. She was also diagnosed with severe constipation, effectively treated with laxation and bowel irrigation. Despite remission of her JIA and constipation, severe fatigue persisted. She was referred to a paediatrician specializing in chronic fatigue. After a standardized diagnostic work-up the diagnosis of chronic fatigue without an identifiable treatable somatic cause was established, and the patient was referred to participate in the FITNET-plus study.

Sarah lived with her mother. Her parents divorced when Sarah was 8 years old. She no longer had contact with her father, nor did her father have legal custody over her. Sarah reported that her main problem was recurrent severe fatigue, but she was also bothered to a lesser extent by persistent pain in shoulders, back and wrist joints without somatic disease activity. She felt distressed and lonely. Fatigue affected her physical and school activities, and social interactions. She became inactive and avoided social activities. She often stayed home for fear of worsening the fatigue. Sarah filled out a set of questionnaires after the intake with the therapist to evaluate the symptom severity, daily limitations and cognitive behavioural fatigue

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perpetuating factors (see Table S1 and paragraph 6.3 in the Supplementary material for the results and interpretation).

Design, procedure and measures

A two-phase A-B SCED was used for a group of nine participants, consisting of a baseline A-phase representing the no-treatment baseline period with weekly measurements of fatigue, pain and disabilities, followed by a B-phase consisting of the intervention and follow-up. The duration of phase A was determined by a computer-generated random number list and varied between 7 and 26 weeks. During the B-phase the weekly measurements were continued. The duration of phase A for Sarah was 8 weeks. Baseline assessments (T0) consisted of two face-to-face sessions in which Sarah also completed questionnaires to identify the perpetuating factors of fatigue. With actigraphy her activity level was assessed for 2 weeks and she also recorded symptoms, bedtimes and activities in a diary during this period. Based on these measurements the following perpetuating factors were identified: a low activity pattern, disturbed sleep-wake rhythm, and a tendency to catastrophize fatigue and JIA. Example of the latter are 'I usually think of everything that could go wrong because of fatigue' or 'JIA makes me feel useless' (see Table S1 and Fig. S1 in Supplementary material).

To evaluate the effect of the intervention, Sarah completed validated self-report outcome measures every week effectively starting 8 weeks before treatment commenced, followed by 26 weekly assessments during treatment, and 16 weekly assessments after completing treatment. After completing the intervention, the baseline measurements were repeated (T1).

Primary outcome measure was fatigue measured with the subscale *fatigue severity* (8 items, 7-point Likert scale) of the Checklist Individual Strength-20 with a range of 8–56 and cut-off score for severe fatigue of 40. Secondary outcomes were the effects of treatment on daily functioning and pain severity. Limitations in daily functioning were measured by (1) *Physical functioning* assessed with the subscale physical functioning (9 items) of the Child Health Questionnaire (CHQ-CF87) (0–100%), and (2) *School absence* expressed in obliged hours minus attended/obliged hours (Albers *et al.*, 2021). *Pain severity* was assessed using the Visual Analogue Scale (VAS) scores for pain (0–100 mm). See Table S1 in the Supplementary material for more details and references to the questionnaires.

Intervention

FITNET-plus builds on FITNET: an established eHealth CBT protocol for ME/CFS in adolescents (Albers *et al.*, 2021) and is enriched with elements of evidence-based CBT protocols for fatigued adults with a chronic medical condition (Goërtz *et al.*, 2021). Clinical interviews with adolescents with IDD gained insight into beliefs and behaviours related to their fatigue and ensured that the content of the treatment portal suited this target group. Based on the interviews, FITNET-plus was extended with a module aimed at coping with pain.

Treatment progression was monitored by regular e-consultations between the therapist, Sarah, and her mother. Medication use for JIA was continued during I-CBT. In case of a disease flare Sarah contacted her rheumatologist and the I-CBT paused until disease remission was achieved (commensurate with the advice of our Ethical Review Board).

Treatment sessions were conducted by a health psychologist with postgraduate training in CBT (L.N.N.), supervised by a clinical psychologist/licensed CBT supervisor (H.K.).

The online platform consisted of eight treatment modules: (1) introduction of I-CBT and psychoeducation, (2) goal setting, (3) regulation of sleep, (4) formulation of helpful beliefs, (5) activity regulation, (6) coping with pain, (7) step-by-step realization of treatment goals, and (8) relapse prevention. The intervention was adjusted to Sarah's individual pattern of perpetuating factors; see Tables S1 and S2 (Supplementary material).

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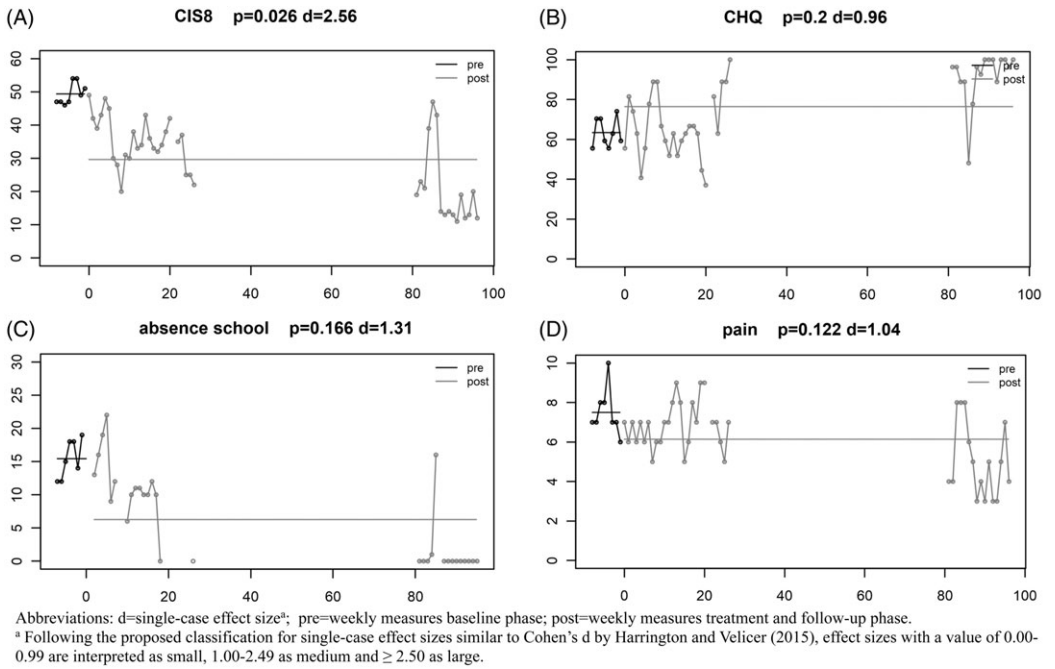

Figure 1. Weekly measures of (A) severity of fatigue, (B) physical functioning, (C) school absence and (D) severity of pain across baseline, treatment and follow-up periods.

The therapist responded online weekly or bi-weekly. For emergency situations, telephone contact details were available to the patient. Sarah's mother had her own online portal with information about how to support Sarah and communicated via email with the therapist.

CBT was provided over a period of 26 weeks and consisted of 17 individual econsultations with Sarah and two econsultations with her mother. No changes in the medical treatment regime for the JIA occurred during the treatment period. Because Sarah was hospitalized for severe constipation in the follow-up period, the weekly follow-up measurements were (in accordance with the study protocol) postponed to disease remission.

Statistical analysis

Single-case weekly assessed longitudinal data (time series) were used to evaluate change. After graphical inspection, changes in mean scores were tested with a one-sided permutation distancing A-B test (PDT), which corrects for dependency of the observations (Houtveen *et al.*, 2022). A one-tailed *p*-value of less than .05 was considered statistically significant. Single-case effect sizes were computed similar to group-level Cohen's *d*, but should be interpreted differently as a result of autocorrelation (<1.00 small, 1.00–2.49 medium, and ≥2.50 large). The feasibility of this intervention was determined with a clinical interview.

Results

Sarah's fatigue was significantly reduced over the course of therapy and follow-up, to below the cut-off for severe fatigue, with a large effect size ($p = .026$, $d = 2.56$; see Fig. 1A). Both physical functioning ($p = .20$, $d = .96$) and school absence ($p = .166$, $d = 1.31$) exhibited improvements during the intervention and follow-up (see Fig. 1B,C), but these effects were not large enough

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to become significant. Pain severity did not reduce materially during the intervention ($p = .122$, $d = 1.04$), although it exhibited a (non-significant) improvement during the follow-up phase (see Fig. 1D).

Sarah's treatment experience

At the post-therapy assessment, Sarah reflected on the treatment period. She described the treatment as helpful in achieving her goals. See the Supplementary material for more detailed information about Sarah's treatment experiences.

Discussion

This case provides preliminary evidence for the feasibility and potential benefits of the application of I-CBT for severe fatigue in an adolescent patient with IDD. The patient showed a significant decrease in fatigue and non-significant changes towards increased school presence and improved physical functioning following I-CBT. I-CBT was well received by the patient with good adherence to treatment; the therapy was helpful in achieving her goals, including reducing the fatigue severity and impairments. The fact that the treatment was available online, thus eliminating the need to travel or skip activities because of therapy, was seen by the patient as a benefit. She did not report a reduction in pain severity, but pain no longer hampered her activities. Importantly, Sarah's progress persisted at follow-up.

These findings offer support for the utility of I-CBT for adolescent patients with chronic medical conditions and is consistent with previous research in adults (Goërtz *et al.*, 2021). This suggests that perpetuating factors such as dysfunctional behaviour have similarities across diseases and could be addressed in a generic transdiagnostic intervention.

We acknowledge that the current report is based on a single-case study, which means it is not certain that the findings can be generalized to other individuals. In addition, a case study is sensitive to idiosyncratic disease related events that influence outcome. Replication in other severely fatigued adolescents with IDD is needed, and is currently being investigated by our group.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1352465822000716.

Data availability statement. The data that support the findings of this study are available from the corresponding author (L.N.N.) upon reasonable request.

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Author contributions. S.L.N. was the principal investigator of this study. L.N.N. was the primary and executive investigator, and was responsible for the acquisition of data and drafting the report. L.N.N., H.K. and J.H. were together responsible for analysis and interpretation of data. S.L.N., E.M.v.d.P. and H.K. designed and supervised the study. J.H., S.L.N., E.M.v.d.P., J.M.v.M. and H.K. revised the manuscript critically. All authors have read and approved the final report.

Linde N. Nijhof: Conceptualization (equal), Data curation (lead), Formal analysis (lead), Funding acquisition (equal), Investigation (lead), Methodology (equal), Project administration (lead), Writing – original draft (lead); **Sanne L. Nijhof:** Conceptualization (lead), Funding acquisition (equal), Investigation (supporting), Methodology (equal), Supervision (supporting), Writing – original draft (supporting), Writing – review & editing (supporting); **Elise M. van de Putte:** Conceptualization (equal), Investigation (supporting), Methodology (equal), Supervision (supporting), Writing – original draft (supporting), Writing – review & editing (supporting); **Jan Houtveen:** Data curation (supporting), Formal analysis (equal), Methodology (equal), Supervision (supporting), Writing – original draft (supporting), Writing – review & editing (supporting); **Joris M. van Montfrans:** Conceptualization (supporting), Funding acquisition (equal), Investigation (supporting), Supervision (equal), Writing – original draft (supporting), Writing – review & editing (supporting); **Hans Knoop:** Conceptualization (equal), Investigation (supporting), Methodology (equal), Supervision (lead), Writing – original draft (supporting), Writing – review & editing (supporting).

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Conflicts of interest. The authors have no competing interests to report.

Ethical standards. This work was conducted in line with the Ethical Principles of Psychologists and Code of Conduct as set out by the American Psychological Association (2017). This study was conducted in accordance with the Declaration of Helsinki and was part of a prospective trial approved by the Ethical Review Board of the University Medical Centre of Utrecht (registration number: 16/237, NL56462.041.16). Written informed consent was obtained for publication of this case study. The work described in this case study was part of scientific research. The participant and her guardian have seen the submission in full and agreed to it going forward for publication. Any information which could potentially identify the participant has been removed or disguised.

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