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To cite this article: Hanna Malmberg Gavelin, Carl-Johan Boraxbekk, Therese Stenlund, Lisbeth Slunga Järholm & Anna Stigsdotter Neely (2015) Effects of a process-based cognitive training intervention for patients with stress-related exhaustion, *Stress*, 18:5, 578-588, DOI: [10.3109/10253890.2015.1064892](https://doi.org/10.3109/10253890.2015.1064892)

To link to this article: <https://doi.org/10.3109/10253890.2015.1064892>



Published online: 13 Aug 2015.



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ORIGINAL RESEARCH REPORT

Effects of a process-based cognitive training intervention for patients with stress-related exhaustion

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Abstract

Stress-related exhaustion has been linked to a pattern of selective cognitive impairments, mainly affecting executive functioning, attention and episodic memory. Little is known about potential treatments of these cognitive deficits. The purpose of this study was to evaluate the effects of a process-based cognitive training intervention, designed to target the specific cognitive impairments associated with stress-related exhaustion. To this end, patients diagnosed with exhaustion disorder (ED) were randomized to either a multimodal stress rehabilitation program with the addition of a process-based cognitive training intervention (training group, $n = 27$) or a treatment-as-usual control condition, consisting of multimodal stress rehabilitation with no additional training (control group, $n = 32$). Treatment effects were evaluated through an extensive cognitive test battery, assessing both near and far transfer effects, as well as self-report forms regarding subjective cognitive complaints and burnout levels. Results showed pronounced training-related improvements on the criterion updating task ($p < 0.001$). Further, evidence was found of selective near transfer effects to updating ($p = 0.01$) and episodic memory ($p = 0.04$). Also, the trained group reported less subjective memory complaints ($p = 0.02$) and levels of burnout decreased for both groups, but more so for the trained group ($p = 0.04$), following the intervention. These findings suggest that process-based cognitive training may be a viable method to address the cognitive impairments associated with ED.

Keywords

Burnout, cognition, executive function, exhaustion disorder, stress rehabilitation, working memory training

History

Received 1 April 2015
Revised 2 June 2015
Accepted 17 June 2015
Published online 13 August 2015

Introduction

Long-term sick-leave due to mental health problems has become an increasing concern in Sweden as well as in other industrialized countries and a large proportion of these sick-leaves are attributable to psychosocial stress (Henderson et al., 2005; Swedish Social Insurance Agency, 2014). One of the most well-known constructs regarding long-term psychosocial stress is burnout – a condition characterized by emotional exhaustion, depersonalization and reduced personal accomplishment (Maslach et al., 2001). Although widely used, the concept of burnout was originally intended to capture critical aspects of the relationship between an individual and their job, rather than a classification of illness. In Sweden, the National Board of Health and Welfare has proposed that the term exhaustion disorder (ED) should be used as a diagnosis in clinical practice, to enable more

systemized diagnostic procedures and rehabilitation measures (refer Table 1 for diagnostic criteria). Burnout and ED are closely related and it has previously been shown that a majority of patients diagnosed with ED also exhibit high levels of burnout (Glise et al., 2012).

A growing body of research has shown that stress-related exhaustion can be linked to a pattern of selective cognitive impairments, mainly affecting executive function, attention and episodic memory (Eskildsen et al., 2015; Jonsdottir et al., 2013; Öhman et al., 2007; Oosterholt et al., 2012; Österberg et al., 2012; Rydmark et al., 2006; Sandström et al., 2005), with impaired executive functioning as the most prominent feature. Notably, even though remaining executive and attentional difficulties have been observed both immediately after treatment and at long-term follow up (Oosterholt et al., 2012; Österberg et al., 2014; Van Dam et al., 2012), prospective follow-up studies are scarce. No study has so far investigated interventions specifically designed to target cognitive impairments in this patient group.

Cognitive performance can be supported in a variety of ways (Wilson, 2008). Recently, process-based cognitive training interventions focusing on executive functioning and

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Table 1. Diagnostic criteria for exhaustion disorder according to the Swedish National Board of Health and Welfare.

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- A. Physical and mental symptoms of exhaustion with minimum of 2 weeks duration. The symptoms have developed in response to one or more identifiable stressors which have been present for at least 6 months.
- B. Markedly reduced mental energy, which is manifested by reduced initiative, lack of endurance or increase of time needed for recovery after mental efforts.
- C. At least four of the following symptoms have been present most of the day, nearly every day, during the same 2-week period:
1. Persistent complaints of impaired memory or concentration.
 2. Markedly reduced capacity to tolerate demands or to work under time pressure.
 3. Emotionally instability or irritability.
 4. Disturbed sleep.
 5. Persistent complaints of physical weakness or fatigue.
 6. Physical symptoms such as muscular pain, chest pain, palpitations, gastrointestinal problems, vertigo or increased sensitivity to sounds.
- D. The symptoms cause clinically significant distress or impairment in occupational, social or other important areas of functioning.
- E. The symptoms are not due to the direct physiological effects of a substance (e.g. drug abuse, medication) or a general medical condition (e.g. hypothyroidism, diabetes, infectious disease).
- F. If criteria for major depressive disorder, dysthymic disorder or generalized anxiety disorder are met, ED is set as co-morbid condition.
-

All capital letters must be fulfilled for the diagnosis.

working memory have attracted much attention (for reviews, see Klingberg, 2010; Morrison & Chein, 2011; Shipstead et al., 2012). Several previous studies have supported the feasibility of process-based cognitive training in healthy adults, showing evidence of training-related improvements in working memory capacity and executive function, as well as indications of the possibilities of broader generalizations of training effects (Chein & Morrison, 2010; Dahlin et al., 2008; Jaeggi et al., 2008; Karbach & Kray, 2009; Sandberg et al., 2014; but see Melby-Lervåg & Hulme, 2013, for a critical review). Regarding clinical populations, some support has been given to the effectiveness of process training for disorders associated with impairments in working memory and executive function, such as depression (Iacoviello et al., 2014; Owens et al., 2013) and acquired brain injury (Åkerlund et al., 2013; Westerberg et al., 2007). However, no studies have yet been conducted with patients diagnosed with ED.

The purpose of this study was to evaluate the effects of a process-based cognitive training intervention, designed to target the specific cognitive impairments associated with ED. We wanted to investigate: (1) whether process-based cognitive training can improve performance on trained cognitive tasks for patients diagnosed with ED, (2) whether potential training effects are generalizable to other, non-trained cognitive tasks and (3) whether process-based cognitive training can reduce subjective cognitive complaints, and patients' levels of burnout.

Methods

Participants

This study was conducted at the Stress Rehabilitation Clinic at the University Hospital in Umeå, Sweden. It was part of a larger randomized controlled trial, Rehabilitation for Improved Cognition (RECO), a parallel, three armed randomized clinical trial evaluating the effects of cognitive training and physical fitness training (indoor cycling) on cognition in patients diagnosed with ED. In this study, we only report data from the group receiving cognitive training relative to the controls. This study was conducted in accordance with the Declaration of Helsinki and approved by the Umeå Regional Ethical Review Board (Dnr 2010-53-31). All participants provided written informed consent prior to the start of the study.

Recruitment was conducted consecutively from April 2010 until June 2013. During this period all patients referred to the Stress Rehabilitation Clinic were screened for eligibility. To speed up the recruitment process, eight participants were also recruited from the Social Insurance Agency in Umeå, Sweden. All patients were initially evaluated by a physician and a psychologist to confirm diagnosis of ED. Inclusion criteria for the study were: (1) confirmed exhaustion disorder according to criteria established by the Swedish National Board of Health and Welfare, (2) 18–60 years of age, (3) current employment, (4) considered by physician and psychologist as suitable for multimodal rehabilitation in group, (5) no known abuse of alcohol or drugs, (6) no need of other treatment or rehabilitation and (7) no participation in other intervention studies. All participants were on sick-leave due to their illness.

Of the 161 patients fulfilling the inclusion criteria, 53 were allocated to the cognitive training group and 46 were allocated to the control group. The remaining 62 patients were allocated to the physical fitness intervention, which will be described elsewhere. Twenty-five patients (47%) discontinued the cognitive training intervention and 13 patients (28%) dropped out of the control condition. Due to large amounts of missing data from the neuropsychological tests, two participants, one from the training group and one control, were removed from the analysis, resulting in a total of 27 individuals in the cognitive training group and 32 individuals in the control group. Demographic and clinical characteristics of the participants are presented in Table 2.

For baseline data, the Shirom–Melamed Burnout Questionnaire (SMBQ) was used to assess level of burnout (Melamed et al., 1992, 1999). The questionnaire consists of 22 items rated on a 7-point Likert scale (1 = “almost never”, 7 = “almost always”). The questionnaire measures different aspects of the burnout syndrome; physical fatigue, emotional exhaustion, tension, listlessness and cognitive weariness. Cronbach's alpha for this questionnaire was 0.94. Further, the Hospital Anxiety and Depression Scale (HAD) was used to assess levels of depression and anxiety (Zigmond & Snaith, 1983). The questionnaire consists of 14 items, seven items targeting depression and seven items targeting anxiety. Each subscale's total score ranges from 0 to 21. Cronbach's alpha was 0.78 and 0.81 for the anxiety and depression subscale, respectively. Participants also

Table 2. Sample characteristics.

Measure	Training group (<i>n</i> = 27)		Control group (<i>n</i> = 32)		<i>p</i>
	Mean	SD	Mean	SD	
Age	44.74	9.11	41.69	7.88	0.17 ^a
Verbal ability	21.15	5.19	23.50	3.51	0.04^a
SMBQ	5.11	0.84	4.84 ^c	1.03	0.28 ^a
HAD depression	7.11	2.68	7.36 ^c	3.61	0.77 ^a
HAD anxiety	11.00	2.76	9.63 ^c	3.91	0.14 ^a
	<i>n</i>	%	<i>n</i>	%	
Sex					0.04^b
Women	20	74	30	94	
Men	7	26	2	6	
Education level					0.15 ^b
Elementary school	3	11	0	0	
High school	9	33	12	37.5	
University	15	56	20	62.5	

Significant group differences are in bold. SMBQ = Shirom–Melamed Burnout Questionnaire.

HAD = Hospital Anxiety and Depression Scale.

^aBased on independent samples *t*-test.

^bBased on Pearson's Chi-square test.

^c*n* = 31.

conducted SRB:1, a multiple-choice synonym test assessing verbal ability (Dureman et al., 1971). The groups were similar in terms of age, educational level, level of burnout, depression and anxiety (p 's > 0.05). However, the cognitive training group had lower verbal ability (p = 0.04) and a larger proportion of men (p = 0.04) than the control group. Drop-out analyses revealed no significant differences in any of the background variables sex, age, educational level, verbal ability, level of burnout, depression or anxiety between patients completing the intervention and those who dropped out.

Procedure

All patients participated in a 24-week multimodal stress rehabilitation program, consisting of (1) weekly 3-h sessions with cognitive behavioral therapy, (2) individual prescription of physical activity and (3) individual vocational measures with rehabilitation meetings. Each rehabilitation group consisted of eight patients. Twenty-two of the weekly sessions were conducted in group and two were individual meetings with the group therapist. The key components of the cognitive behavioral program were: education (e.g. stress reactions, sleep, affect, medication, the importance of rest in order to recover), awareness of reactions and ‘self-talk’, development of behavioral-, cognitive- and emotional skills, spiritual issues and life values and developing strategies for returning to full-time work. After 12 weeks of rehabilitation, a randomization by rehabilitation group was conducted to one of three conditions; (1) multimodal rehabilitation with no additional training, (2) multimodal rehabilitation with the addition of computerized process-based cognitive training and (3) multimodal rehabilitation with the addition of physical fitness training (indoor cycling). The added training was performed during the last 12 weeks of multimodal rehabilitation, with three weekly training sessions. Due to high drop-out rates in both training groups, the randomization was adjusted in the latter part of the study with a doubled possibility of allocation to these groups compared to the control condition.

Psychological variables and physical fitness were assessed before the multimodal stress rehabilitation program (Baseline), before randomization (T1) and at the end of the rehabilitation program (T2). At T1 and T2, patients also completed a cognitive test battery and completed self-report forms regarding subjective cognitive complaints. The cognitive test battery was administered in two sessions, approximately 1 h each. Most participants performed the sessions at one occasion, separated by a 15-min break. If necessary, the sessions were conducted at two separate occasions. The tests were administered in a standardized sequence (see below) and tests with parallel forms were counterbalanced between T1 and T2. Due to miscommunication, not all participants were administered the self-report forms regarding subjective cognitive complaints. This problem was constrained to a limited time during the data collection and mainly affected the control group. All participants received a compensation of 600 SEK (approximately 60 Euro).

Intervention

The cognitive training program was developed to target the cognitive functions and related brain areas known to be sensitive to prolonged periods of stress exposure. Two brain regions particularly vulnerable to stress are the prefrontal cortex and the hippocampus (Lupien et al., 2009). These brain areas are central for episodic- and working memory as well as executive functions. Hence, our program addressed these three functions by letting the participants practice on six cognitive tasks. Two tasks targeted the executive processes updating and shifting, respectively (Miyake & Friedman, 2012). A visuospatial span task was used to tap short-term memory and a word-associate task was used to address episodic memory binding. All these tasks have previously been used in our cognitive training research with positive results (Dahlin et al., 2008; Ngandu et al., 2015; Sandberg et al., 2014).

During the first week, patients were instructed and performed the training at the Stress Rehabilitation Clinic.

Thereafter, the computerized training continued at home, using a web-based program. Each training session was approximately 15–20 min long and performed three times a week, a total of 36 sessions. All answers were given with the computer keyboard or mouse and feedback on task performance was given after each task. All tasks were adaptive, except for the shifting tasks (see below), so that when a participant reached 80% correct answers in one level, they moved up to a more difficult level. Thus, training remained challenging, as a way of maximizing engagement of executive functions while minimizing automatic processes and use of task-specific strategies.

Updating

In Letter memory running span (Miyake et al., 2000), five list of single letters was presented serially in the center of the computer screen at a rate of 2 s/letter. After presentation, the letters were outlined at the bottom of the screen and participants were asked to recall the four last presented letters in the correct order, by clicking on the letter with the computer mouse. The level of difficulty was adjusted when the participant scored at 80% correct. Difficulty level was determined by varying the list-lengths as follows: low level = 4–7 items; medium level = 6–11 items; high level = 5–15 items, where the low level was considered less cognitively taxing due to less number of updates.

In the Keep track task (Miyake et al., 2000; Yntema, 1963), three trials of 15 words per trial, belonging to different semantic categories, were presented serially at a rate of 2 s/word. At the bottom of the computer-screen, semantic category-boxes (e.g. clothes, animals, relatives and sports) were displayed. The task was to mentally place the word presented in the correct category-box and continually update the content of the box to be able to recall the last word mentally placed in the box. Some words did not belong to any category-box. When the participant recalled 80% correct, the next difficulty level was presented. The level of difficulty was manipulated by varying the number of categories (boxes) presented, with three (low), four (medium) or five (high) target categories, respectively.

Shifting

In alternating runs with digits (Rogers & Monsell, 1995), participants were asked to classify digits (1, 2, 3, 4, 6, 7, 8 or 9) as odd/even or lower/higher than five, depending on their position in a square. The digits were presented in the square in a clockwise manner. Background color (blue or pink) served as additional cues. Also, an unpredictable task cuing paradigm was used (Rogers & Monsell, 1995), where participants were asked to classify letters (A, B, D, E, X, Y, U or Z) as beginning/end of the alphabet or vowel/consonant, depending on the cue accompanying every trial (blue square or red circle). These tasks were alternated between sessions and were not adaptive.

Visuospatial short-term memory

In the Visuospatial span task, a four-by-four grid of green squares was presented. The squares turned red one-by-one for

1 s/square and the participant was asked to recall the sequence in correct order by clicking with the computer mouse. Nine trials were presented and the task was adaptive to the performance of the subject, so when two correct trials out of three were reached the next span-level was presented, but if not reached a lower span-level was presented.

Episodic memory

In the three-word-associates task, the participants were presented with a list of 12 triplets depicting a location, an object and a color, such as “airport-ant-pink”. The task was to associate the three to-be-remembered words, such as imagining a pink ant at the airport. At retrieval, the participants were given the location as a cue and were asked to recognize the object and the color in a multiple-choice format. The task was adaptive by decreasing the presentation time when the performance reached 80% correct starting with 8 s/triplet, then 5 s and finally 3 s/triplet.

Cognitive tests

The cognitive test battery consisted of 11 tests, with a varying degree of overlap with the abilities addressed in training. The tests were divided into three categories: criterion tests – the same tasks as used in the training program, measuring training gains; near transfer tests – tasks not used in the training program, but targeting the same abilities as those trained; and far transfer tests – tasks measuring other, untrained abilities.

In order to limit the time required to complete the pre- and post-test sessions, two of the five training tasks were chosen as criterion tests (Letter memory running span, Visuospatial span task). These tests were chosen to facilitate comparisons with our previous work (Dahlin et al., 2008; Sandberg et al., 2014) as well as others. However, due to technical problems, data from the Visuospatial span task could not be included in the analysis. Letter memory running span was administered using a similar procedure as during training. In contrast to the training program, however, the task consisted of 10 lists instead of five and answers were given using four adjacent keys on the computer keyboard with the corresponding letters taped over the keys. Also, answers on the criterion task version were timed, giving participants 6 s to respond. List lengths were unknown to the participants and varied between seven and 15 items. For a detailed description of the criterion task procedure for this task, see Sandberg et al. (2014). The dependent measure was number of correctly recalled four-letter sequences. Two different versions of the test were used and counterbalanced between T1 and T2.

The *n*-back task was used to assess near transfer to updating. For a detailed description of this task, see Sandberg et al. (2014). In this task, numbers were presented serially in the middle of the computer screen. Three different conditions were presented: 1-back, 2-back and 3-back and for each condition participants were required to judge whether the number presented was the same as the one that appeared one, two or three stimuli previously. In total, 27 sequences, nine of each condition, were alternated during the test. Performance was measured in number of hits minus false alarms in each condition and the results from the 3-back task were used as dependent measure.

The Color-word interference test (also known as the Stroop test) from D-KEFS was used to assess near transfer to inhibition (Delis et al., 2001). In condition one, participants were asked to name a set of red, blue or green color patches as quickly as possible. In condition two, they were asked to read color words presented in black ink (e.g. *red*, *blue*). In condition three, they were required to state the color of color words printed in an incongruent color (e.g. the word *red*, printed in a green color). An inhibition cost was calculated, i.e. time taken (seconds) to complete incongruent trials as compared to reading color words.

To assess near transfer to shifting, two conditions from the Trail making test (TMT) from D-KEFS were used (Delis et al., 2001). Participants were presented with circles containing letters and numbers and asked to connect the circles containing numbers in numerical order (TMT part 2) and to alternate between numbers and letters according to numerical and alphabetical order (TMT part 4). A shift cost was calculated, i.e. the difference in time (seconds) taken to complete TMT part 4 as compared to TMT part 2.

Three tests were used to assess near transfer to short-term and working memory. In Digit span from WAIS-R (Wechsler, 1981), participants were asked to recall digits forwards or backwards. Two different versions were used and counterbalanced between participants. In Letter-number sequencing, adapted from WAIS-III (Wechsler, 1997), participants were presented with a series of letters and numbers and asked to recall the numbers in numerical order followed by the letters in alphabetical order. Performance was measured in number of correctly recalled sequences for Digit span forwards, Digit span backwards and Letter-number sequencing, respectively.

To assess near transfer to episodic memory, a list of 18 concrete nouns was used as a free-recall task. The list was in-house developed and administered according to Buschke's (1973) selective reminding procedure. Participants were initially presented with the list on a computer screen, at the rate of five seconds per item, followed by a free-recall test. On subsequent trials, words not successfully recalled were re-presented verbally to the participants. After each presentation, participants were asked to recall the complete list again. The list was presented four times and total number of recalled items across all four trials was used as outcome measure. Three parallel versions were used and counterbalanced between T1 and T2.

Digit symbol from WAIS-R (Wechsler, 1981) was used to assess far transfer to perceptual speed. Participants were required to draw as many symbols as possible into empty boxes, according to a number coding key. Number of items completed in 90 s was used as outcome measure.

Raven et al.'s (1998) advanced progressive matrices was used to assess far transfer to non-verbal reasoning ability. Participants were presented with 3 × 3 pattern matrices in which one part of the pattern was missing. They were then required to determine which one of eight different pieces best fit the missing part. The test consists of 36 items. It was split into two parts using odd and even items and the two versions were counterbalanced between T1 and T2. Number of correctly completed items in 10 min was used as outcome measure.

The cognitive tests were administered in the following standardized sequence: Digit symbol, Letter memory running span, Digit span forwards, Digit span backwards, Color-word interference test, TMT, SRB:1 (only administered at T1), the *n*-back task, Letter-number sequencing, Raven's matrices, Recall of concrete nouns and the Visuospatial span task.

Subjective cognitive complaints

The 6-item Questionnaire of Everyday Memory Problems (6-QEMP) was used to assess memory problems in daily life. The questionnaire consists of six items. Three items ['Does anyone close to you (family, friends) think you have a poor memory?'; 'Do you forget appointments if not prompted by someone else or by a reminder such as a calendar or a diary?'; 'Does it occur that you do not remember things that have recently happened?'] were rated on a 5-point Likert scale for which 1 = "never" and 5 = "very often". The three remaining items ('How is your memory today, in comparison with your memory before your stress-related illness?'; 'How is your memory today, in comparison with when you had the most problems with your stress-related illness?'; 'How do you perceive your memory in comparison with that of other persons your age?') were rated on a 5-point Likert scale for which 1 = "much better" and 5 = "much worse". Cronbach's alpha for this measure was 0.64. A five-item version of this questionnaire has previously been used on patients with stress-related exhaustion (Öhman et al., 2007; Österberg et al., 2014).

The Prospective and Retrospective Memory Questionnaire (PRMQ) was used to assess subjective memory complaints (Crawford et al., 2003). The PRMQ consists of 16 items regarding memory slips in everyday life, eight asking about prospective memory failures (e.g. "Do you decide to do something in a few minutes time and then forget to do it?") and eight asking about retrospective memory failures (e.g. "Do you fail to recognize a place you have visited before?"). Answers are given on a 5-point Likert scale (1 = "never", 5 = "very often"). Since it has been indicated that patients with stress-related exhaustion may have specific problems concerning prospective memory (Eskildsen et al., 2015; Öhman et al., 2007), results on the prospective- and retrospective subscale of the PRMQ were analyzed separately. Cronbach's alpha was 0.88 and 0.83 for the prospective and retrospective subscale, respectively.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics version 22 (SPSS Inc., Chicago, IL). Power calculations were conducted based on results from a previous pilot study, in which patients with ED improved their performance on the criterion updating task Letter memory running span from 3.0 (±1.4) pre-test to 5.8 (±1.9) post-test. Based on these results, 30 participants in each group would give an 80% power to detect a statistically significant difference with a two-sided 5% significance level.

All analyses were conducted by per protocol, including only participants who completed the 12-week intervention period. For baseline characteristics, differences between the groups were analyzed using independent samples *t*-test for

continuous variables and Pearson's Chi-square tests for categorical variables. Change in levels of burnout following the intervention period was evaluated by conducting a 2 (Group: Training versus Control) \times 2 (Time: T1 versus T2) mixed ANOVA. In all analyses, evaluating treatment effects on cognitive test performance and levels of subjective cognitive complaints, age, sex and verbal ability were treated as covariates in order to adjust for baseline differences between the groups. We used centered covariates in line with recommendations by Van Breukelen & Van Dijk (2007). In order to investigate the effect of treatment on overall cognitive functioning, a 2 (Group: Training versus Control) \times 2 (Time: T1 versus T2) mixed MANCOVA was performed, including the nine transfer tasks as dependent variables. For each cognitive test and the measures of subjective cognitive complaints, 2 (Group: Training versus Control) \times 2 (Time: T1 versus T2) mixed ANCOVA's were conducted. Significant interaction effects were further qualified by Bonferroni *post hoc* pairwise comparisons. For effect size estimates, partial eta squared (η_p^2) was used for main and interaction effects and Cohen's *d* was used for pre-test to post-test change in each group, respectively.

An imputation procedure was used to replace missing responses on single items, using the expectation-maximization method. For the cognitive tests, this was done for three participants who were missing single test results. For the measures of subjective cognitive complaints, three items (0.23%) were imputed on the PRMQ and five items (0.97%) on the 6-QEMP. Participants missing responses to more than two items on the PRMQ and more than one item on the 6-QEMP were excluded from analysis.

Results

Cognitive test performance

Group means and standard deviations for the cognitive tests are presented in Table 3, along with interaction effect statistics. There were no significant differences between the cognitive training group and the control group in baseline performance on the criterion or transfer tests (p 's > 0.05).

Training gains in the criterion task

For Letter memory running span, results from the ANCOVA revealed a significant main effect of Time, $F(1, 54) = 31.51$, $p < 0.001$, $\eta_p^2 = 0.37$, and of Group, $F(1, 54) = 8.83$, $p < 0.01$, $\eta_p^2 = 0.14$, showing that overall performance was higher at T2 than at T1 and that the cognitive training group performed higher than the control group. More importantly, there was a significant Group \times Time interaction $F(1, 54) = 22.00$, $p < 0.001$, $\eta_p^2 = 0.29$. *Post hoc* tests showed that the training group improved significantly from T1 to T2 ($p < 0.001$), whereas no significant change was found for the control group ($p = 0.70$).

Effects of training on overall cognitive functioning

Results from the MANCOVA revealed a significant main effect of Time, $\lambda = 0.39$, $F(9, 46) = 8.06$, $p < 0.001$, $\eta_p^2 = 0.61$. There was no significant main effect of Group ($p = 0.70$). More importantly, a significant Group \times Time interaction was found, $\lambda = 0.66$, $F(9, 46) = 2.61$, $p = 0.02$, $\eta_p^2 = 0.34$, showing that change across sessions in overall cognitive function, as measured by the nine transfer tests, varied between the two groups.

Near transfer tests

For the near transfer tests, results from the ANCOVA's revealed a significant main effect of Time for the 3-back task, $F(1, 54) = 20.21$, $p < 0.001$, $\eta_p^2 = 0.27$, Inhibition cost, $F(1, 54) = 22.89$, $p < 0.001$, $\eta_p^2 = 0.30$, and Digit span backwards, $F(1, 54) = 5.22$, $p = 0.03$, $\eta_p^2 = 0.09$, revealing that overall performance for these cognitive tests improved from T1 to T2. No significant main effects of Time were found for the remaining near transfer tests (p 's > 0.05). Further, there were no significant main effects of Group (all p 's > 0.05). More importantly, a significant Group \times Time interaction effect was found for the 3-back task, $F(1, 54) = 7.43$, $p = 0.01$, $\eta_p^2 = 0.12$. *Post hoc* tests showed that the training group improved significantly from T1 to T2 ($p < 0.001$), whereas the control group showed no significant change ($p = 0.28$). Further, a significant Group \times Time interaction was found for Recall of concrete nouns, $F(1, 54) = 4.57$, $p = 0.04$, $\eta_p^2 = 0.08$. *Post hoc*

Table 3. Group means, standard deviations and interaction effect statistics on criterion-, near transfer- and far transfer tests.

Measure	Training group		Control group		ANCOVA Group \times Time		
	T1	T2	T1	T2	F	<i>p</i>	η_p^2
Criterion test							
Letter memory running span	2.30 (1.64)	4.72 (1.86)	2.24 (1.63)	2.37 (1.84)	$F(1, 54) = 22.00$	< 0.001	0.29
Near transfer tests							
3-back	20.28 (6.00)	25.93 (5.61)	23.42 (5.96)	24.59 (5.57)	$F(1, 54) = 7.43$	0.01	0.12
Inhibition cost	31.50 (10.90)	24.40 (8.18)	27.33 (10.82)	24.07 (8.12)	$F(1, 54) = 2.67$	0.11	0.05
Shift cost	49.96 (26.97)	43.30 (25.76)	46.97 (26.79)	41.63 (25.59)	$F(1, 54) = 0.03$	0.87	0.00
Digit span forwards	7.05 (2.22)	7.59 (1.90)	7.21 (2.21)	6.97 (1.88)	$F(1, 54) = 3.03$	0.09	0.05
Digit span backwards	6.72 (2.17)	7.34 (1.89)	5.99 (2.16)	6.42 (1.87)	$F(1, 54) = 0.14$	0.71	0.00
Letter-number sequencing	10.14 (2.61)	10.75 (2.31)	10.35 (2.59)	9.91 (2.30)	$F(1, 54) = 2.14$	0.15	0.04
Recall of concrete nouns	52.39 (10.30)	57.05 (12.27)	53.05 (10.24)	51.97 (12.19)	$F(1, 54) = 4.57$	0.04	0.08
Far transfer tests							
Digit symbol	53.36 (11.06)	59.27 (13.03)	54.58 (10.98)	58.12 (12.94)	$F(1, 54) = 1.66$	0.20	0.03
Raven's matrices	6.75 (2.66)	7.74 (2.42)	7.12 (2.64)	5.91 (2.40)	$F(1, 54) = 6.80$	0.01	0.11

Means and standard deviations are adjusted for age, sex and verbal ability. Significant Group \times Time interaction effects are in bold.

tests showed that the training group significantly improved their episodic memory performance from pre- to post-test ($p=0.02$), but no significant change was seen in the control group ($p=0.54$). No significant Group \times Time interactions were found for the remaining near transfer tests, i.e. Inhibition cost, Shift cost, Digit span forwards, Digit span backwards or Letter-number sequencing (p 's ranging from 0.09 to 0.87).

Far transfer tests

Results from the ANCOVA revealed a significant main effect of Time for Digit symbol, $F(1, 54)=30.75$, $p<0.001$, $\eta_p^2=0.36$, showing that overall performance improved from T1 to T2. Neither significant main effect of Time was found for Raven's matrices, nor were there any significant main effects of Group on any of the far transfer tests (p 's >0.05). Further, a significant Group \times Time interaction was found for Raven's matrices, $F(1, 54)=6.80$, $p=0.01$, $\eta_p^2=0.11$. *Post hoc* tests revealed that the control group significantly decreased their performance from T1 to T2 ($p=0.03$). The training group participants showed some improvement in their performance from T1 to T2, but this effect did not reach statistical significance ($p=0.11$). No significant Group \times Time interaction was found for Digit symbol ($p=0.20$).

Figure 1 shows effect sizes expressed in Cohen's d for all cognitive tests.

Subjective cognitive complaints

Group means and standard deviations for the measures of subjective cognitive complaints are found in Table 4, along with interaction effect statistics. Since not all participants were administered the self-report forms regarding subjective cognitive complaints, results in this section are based on a

subset of the complete sample (refer Table 4 for information about number of participants on each measure in the cognitive training and control group, respectively). There were no significant baseline differences in levels of subjective cognitive complaints between the groups (all p 's >0.05). Results from the ANCOVA's revealed a significant main effect of Time for the 6-QEMP, $F(1, 38)=5.74$, $p=0.02$, $\eta_p^2=0.13$, and for the PRMQ prospective scale, $F(1, 36)=12.25$, $p=0.001$, $\eta_p^2=0.25$, showing that overall levels of subjective cognitive complaints decreased from pre- to post-test on these measures. No significant main effect of Time was found for the PRMQ retrospective scale ($p=0.22$). Further, results revealed no significant main effects of Group (all p 's >0.05). More importantly, a significant Group \times Time interaction was found on the 6-QEMP, $F(1, 38)=6.32$, $p=0.02$, $\eta_p^2=0.14$. *Post hoc* tests showed that the training group reported significantly fewer everyday memory problems from T1 to T2 ($p<0.001$), whereas no significant change was seen in the control group ($p=0.81$). No significant Group \times Time interaction was found on the PRMQ Prospective scale ($p=0.11$) or the PRMQ Retrospective scale ($p=0.48$).

Effect sizes expressed in Cohen's d for the measures of subjective cognitive complaints are shown in Figure 2.

Levels of burnout

Results on the SMBQ revealed a significant main effect of Time, $F(1, 56)=36.89$, $p<0.001$, $\eta_p^2=0.40$, showing that the overall level of burnout decreased from pre- to post-test. No significant main effect of Group was found ($p=0.87$). Further, there was a significant Group \times Time interaction effect, $F(1, 56)=4.54$, $p=0.04$, $\eta_p^2=0.08$. *Post hoc* tests showed that the training group participants improved

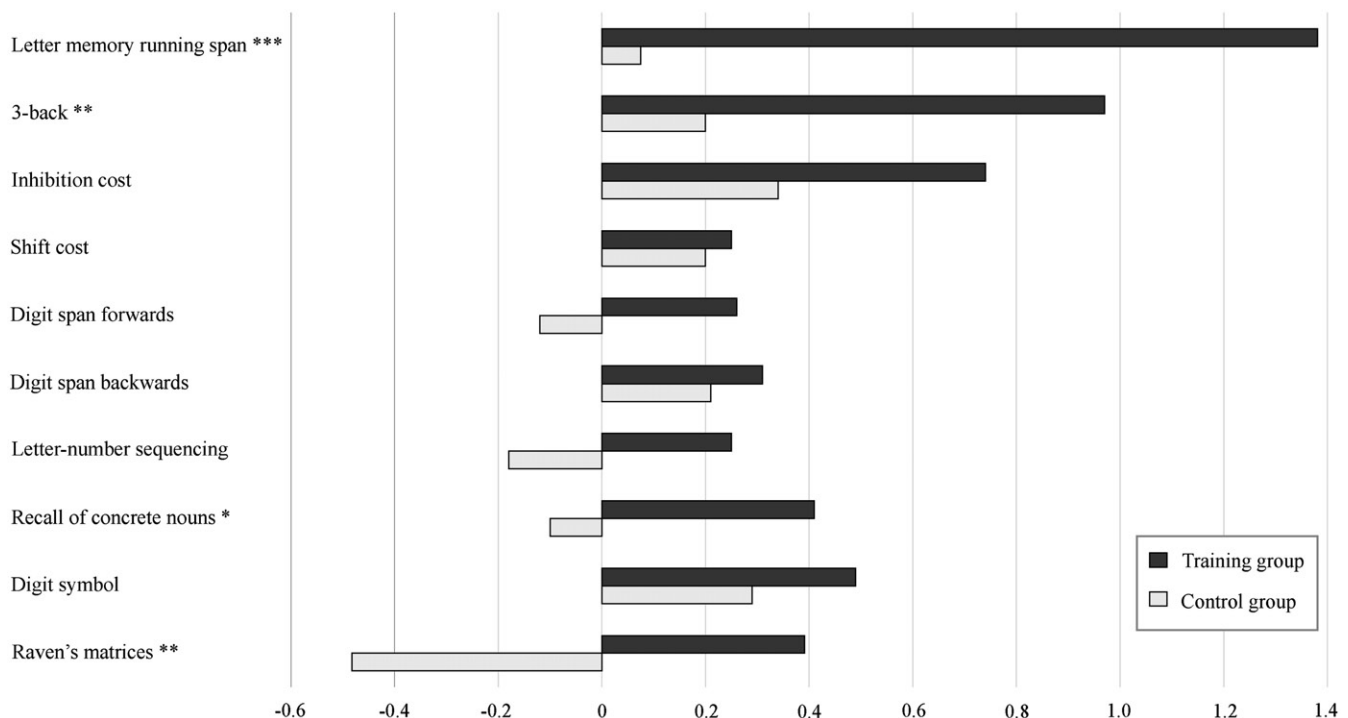


Figure 1. Effect sizes in Cohen's d ($M_{\text{post}} - M_{\text{pre}} / \sqrt{[(SD_{\text{post}}^2 + SD_{\text{pre}}^2) / 2]}$) for all cognitive tests, based on pre-test to post-test change for the training group and the control group, respectively. Positive values represent an improvement. Significant interaction effects are denoted * $p<0.05$; ** $p<0.01$; *** $p<0.001$.

Table 4. Group means, standard deviations and interaction effect statistics on self-report forms regarding subjective cognitive complaints.

Measure	<i>n</i>	Training group		<i>n</i>	Control group		ANCOVA Group \times Time		
		T1	T2		T1	T2	F	<i>p</i>	η_p^2
6-QEMP	26	3.47 (0.59)	3.01 (0.72)	17	3.48 (0.60)	3.51 (0.74)	F(1, 38) = 6.32	0.02	0.14
PRMQ Prospective	24	26.27 (6.71)	23.24 (6.41)	17	26.91 (6.82)	25.95 (6.52)	F(1, 36) = 2.73	0.11	0.07
PRMQ Retrospective	24	20.56 (6.81)	19.58 (6.07)	17	22.28 (6.93)	22.06 (6.18)	F(1, 36) = 0.51	0.48	0.01

Means and standard deviations are adjusted for age, sex and verbal ability. Significant Group \times Time interaction effects are in bold. 6-QEMP = 6-item Questionnaire of Everyday Memory Problems; PRMQ = Prospective and Retrospective Memory Questionnaire.

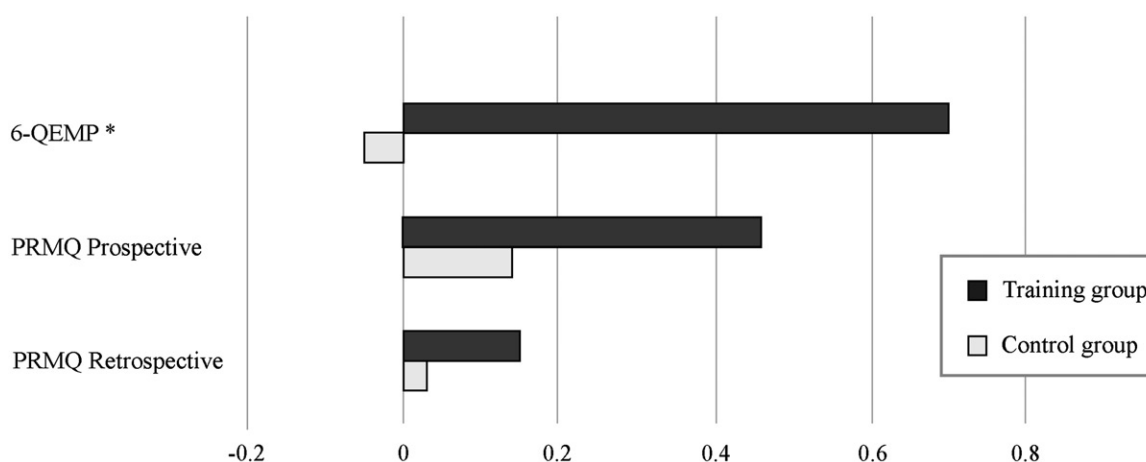


Figure 2. Effect sizes in Cohen's d ($M_{\text{post}} - M_{\text{pre}} / \sqrt{[(SD_{\text{post}}^2 + SD_{\text{pre}}^2)/2]}$) for the measures of subjective cognitive complaints, based on pre-test to post-test change for the training group and the control group, respectively. Positive values represent an improvement. 6-QEMP = 6-item Questionnaire of Everyday Memory Problems; PRMQ = Prospective and Retrospective Memory Questionnaire. Significant interaction effects are denoted * $p < 0.05$.

significantly from pre- to post-test [mean 5.11 (SD = 0.84) at pre-test, compared with mean 4.21 (SD = 1.14) at post-test, $p < 0.001$], as did the control group [mean 4.84 (SD = 1.03) at pre-test, compared with mean 4.41 (SD = 1.10) at post-test, $p < 0.01$]. Hence, both groups showed decreased levels of burnout from pre- to post-test, but the magnitude of improvement was larger for the cognitive training group than for the control group.

Discussion

This study evaluated the effects of a process-based cognitive training intervention, targeting executive function, working memory and episodic memory in a clinical population of patients diagnosed with ED. We wanted to evaluate the effects of the intervention on both trained and non-trained cognitive tasks, as well as on levels of subjective cognitive complaints and burnout symptoms. Results showed substantial training-related improvements on a trained updating task, as well as evidence of selective near transfer effects. Further, some support was given for fewer subjective memory complaints and decreased levels of burnout for the trained group following the intervention.

After the 12-week cognitive training intervention, the training group participants showed substantial improvements on the criterion test, Letter memory running span, indicating a robust training-related improvement on this task. These results are in line with previous research supporting the modifiability of executive functions in healthy adults and clinical groups such as depression and traumatic brain injury

(Iacoviello et al., 2014; Owens et al., 2013; Sandberg et al., 2014; Westerberg et al., 2007). Importantly, this study extends previous findings, showing that training of executive function is possible also for patients diagnosed with ED.

This study included an extensive cognitive test battery, designed to have a varying degree of overlap with the abilities addressed in training, in order to assess both near and far transfer. Results on the near transfer tests revealed a large training-related improvement on the 3-back task. Similar transfer effects have previously been shown following updating training in healthy young individuals (Bäckman et al., 2011; Dahlin et al., 2008). Since the training and transfer updating tasks differed on several dimensions, it is reasonable to assume that the improvement in 3-back performance seen in the cognitive training group may reflect an improvement in the underlying updating function, rather than a specific skill acquisition. To note here is that the training group also improved on the short-term memory task, Digit span forwards, although the interaction effect fell short of significance. The abilities related to hold and update working memory representations may be of particular importance to this patient group, as these abilities have repeatedly been found to be impaired in patients with stress-related exhaustion (Eskildsen et al., 2015; Jonsdottir et al., 2013; Öhman et al., 2007; Oosterholt et al., 2012; Rydmark et al. 2006; but see also: Oosterholt et al., 2014).

Further, near transfer was also shown for the episodic memory task, Recall of concrete nouns. We administered this task according to the selective reminding procedure, which requires participants to continuously keep track of both

presented words as well as words previously recalled and therefore not re-presented, suggesting that updating of memory representations may be involved in task performance. These findings are in keeping with prior results by Dahlin et al. (2008), who also found evidence of transfer to both 3-back and Recall of concrete nouns following updating training. It has previously been hypothesized that the memory impairments exhibited by patients with ED could be due to executive dysfunction and inefficient strategy implementation (Eskildsen et al., 2015; Öhman et al., 2007). Therefore, strengthening of executive control processes may be a key feature in reaching generalizations of training effects to episodic memory (Brehmer et al., 2011). In addition, the finding of improved episodic memory performance for the trained group may also be accounted for by more efficient mnemonic strategies, as the training emphasized binding skills that can be applied in the episodic memory transfer task. Finally, no evidence of near transfer was found for the remaining measures, i.e. inhibition, shifting and working memory tasks.

Regarding far transfer measures, a significant interaction effect was found for Raven's matrices. These results are of particular interest, since the theoretical justification for process-based training of executive functions and working memory is the relationship between working memory and higher order cognitive functions, such as fluid intelligence (Engle et al., 1999; Kane et al., 2005). However, previous studies attempting to validate these theoretical claims, by investigating if cognitive training could lead to gains on fluid reasoning tasks, have shown somewhat inconsistent results (Au et al., 2015; Karbach & Kray, 2009; Redick et al., 2013; Sandberg et al., 2014). In our study, a small improvement was observed in the cognitive training group on Raven's matrices (Cohen's $d = 0.39$), however, this effect did not reach statistical significance. Further, interpretations are complicated by the fact that the control group significantly decreased performance from pre- to post-test. Hence, these results are unclear and this initial study needs to be replicated in order to further clarify the potential effects of process-based cognitive training on reasoning ability for patients with ED.

Although speculative, one possible explanation for the decreased performance observed in the control group could be attributable to fatigue effects, since Raven's matrices was one of the last tasks administered during the 2-h test session. Notably, the control group showed a decrease in pre- to post-test performance on four tests, three of which were conducted in the final part of the session. Since patients with stress-related exhaustion experience problems with mental fatigue when conducting cognitive tasks (Oosterholt et al., 2014; Van Dam et al., 2011, 2012), as well as when having returned to work after stress rehabilitation (Stenlund et al., 2012), an interesting avenue for future research might be to investigate the effects of cognitive training on cognitive sustainability in this patient group.

In this study, results on the measures of subjective cognitive complaints revealed a significant treatment effect on the 6-QEMP, indicating that the cognitive training group reported fewer everyday memory problems following the intervention. The improvement in the cognitive training group was of medium effect size (Cohen's $d = 0.70$). Regarding the

PRMQ, no significant improvement was seen in the training group relative to the controls on the prospective- or retrospective subscale. However, it should be noted that the result on the PRMQ Prospective scale was not far from significant and that the effect size for the improvement in the cognitive training group was moderate. It is possible that the study was inadequately powered to detect a statistically significant treatment effect, due to the small number of participants on these measures. Nevertheless, these results are interesting since the ability to remember to execute an intended action in the future is reliant on executive control processes and plays an important role in everyday memory functioning (McDaniel et al., 1999). Finally, results on the SMBQ showed that in both groups, levels of burnout decreased following the rehabilitation period. However, the cognitive training group showed a larger improvement in burnout symptoms than did controls. Taken together, the effects of the cognitive training intervention on the patients' daily life are promising and future research should more thoroughly investigate the clinical relevance of cognitive training for this patient group, including its potential effects on work ability. This may be of particular importance considering that attending work while ill (e.g. presenteeism) has been associated with reduced on-the-job productivity across a variety of physical and mental health conditions (Johns, 2010). The relation between cognitive functioning following rehabilitation from stress-related illness and work ability should directly be addressed in future studies. As follow-up data collection is currently on-going, we will be able to address the prolonged effects of cognitive training for stress-related rehabilitation when returning to work.

Some limitations of this study need to be addressed. First of all, the study suffered from high attrition rates. To note is that there were no systematic differences in baseline characteristics between patients participating in the intervention and those who dropped-out. However, the large amount of drop-outs implicates that there may be some constraints to the generalizations of study results. The training program requires investment of both time and effort and since one of the core symptoms of ED is exhaustion, training might be overly strenuous for some individuals. A potential way to address this issue in the future could be to include ratings of patients' levels of fatigue and motivation continuously during the intervention period.

A second limitation is the fact that the study did not use a placebo control and no concealment was possible. Thus, we cannot exclude that motivational factors and expectancy effects could be responsible for improvements in the outcome measures. On the other hand, a strength of the study is the fact that both groups actively participated in the multimodal rehabilitation program during the intervention period, making treatment effects less likely to be attributable to factors such as social contact or differential attention to participants.

Finally, this study used an extensive cognitive test battery in order to carefully examine both near and far transfer effects. The downside of this approach is the risk of chance findings due to the large number of analyses carried out, as we chose not to correct for multiple comparisons due to the increased risk of making a Type II error. However, the general trend of improvement observed in the cognitive training

group, as confirmed by the significant Group \times Time interaction on the multivariate test, lends some support to the notion that the transfer effects observed in this study are not simply due to chance, but rather reflects some training-related improvement in cognitive functioning. Future studies should investigate whether there are individual differences as to which patients might benefit from cognitive training as part of their stress rehabilitation. Moreover, it is also of interest to include long-term follow-ups, in order to investigate whether training effects are maintained over time.

Conclusions

In conclusion, the results from this study suggest that process-based cognitive training may be a viable method to address the cognitive impairments associated with ED. Of particular importance were the transfer effects observed in this study, extending beyond the specific tasks used in the training program, suggesting that the effects of the training were generalizable. Considering the importance of executive functioning in complex tasks, even minor improvements could have an impact on an individual's everyday life – especially when attempting to rehabilitate and return to work after sick-leave. Therefore, cognitive training may be an important part of the rehabilitation of ED.

Acknowledgements

We thank Tony Qwillbard for programming the internet-based cognitive training program used in this study and Sofia Nording, Ingela Aronsson, Sofia Levin, Erik Karlsson and Maja Agnemo for valuable assistance in data collection. These data have been presented at the International Convention of Psychological Science in Amsterdam, Netherlands in March 2015 and are part of Hanna M G's dissertation.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article. This research was supported by a grant from the Swedish Research Council for Health, Working life and Welfare, the Swedish Social Insurance Agency (REHSAM), the Västerbotten County Council and the Graduate School in Population Dynamics and Public Policy at Umeå University.

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