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Mental fatigue, cognitive performance and autonomic response following sustained mental activity in clinical burnout

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A R T I C L E I N F O

Keywords:
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Cognition
Exhaustion disorder
Heart rate variability
Mental fatigue

A B S T R A C T

Objective: To investigate the effects of sustained mental activity on perceptions of mental fatigue, cognitive performance, and autonomic response in patients with clinical burnout as compared to a healthy control group.
Methods: Patients with clinical burnout (n = 30) and healthy control participants (n = 30) completed a 3-hour test session, in which they were administered a set of cognitive tests before and after an effortful cognitive task with concurrent sound exposure. Perceptions of mental fatigue and task demands (mental effort and concentration difficulties) were assessed repeatedly over the course of the test session. Heart rate variability was recorded to index autonomic response.
Results: In comparison with controls, perceived mental fatigue increased earlier in the session for the clinical burnout group and did not recover following a short rest period. Throughout the session, patients rated the tasks as more demanding and showed less improvement on measures of attention and processing speed, inhibition and working memory. While autonomic responses were initially comparable, there was a unique decrease in high-frequency heart rate variability in the clinical burnout group after extended testing and exposure.
Conclusion: Patients with clinical burnout are affected differently than healthy controls by sustained mental activity, as reflected by ratings of perceived mental fatigue, aspects of cognitive performance and autonomic response. Further investigation into the role of autonomic regulation in relation to cognitive symptoms in clinical burnout is warranted.

1. Introduction

Mental health problems are leading cause for disability in many countries and psychosocial stress exposure at work has been identified as a key risk factor for the development of depression, anxiety, and stress-related disorders (Harvey et al., 2017). One well-known consequence of long-term psychosocial stress is burnout, a multidimensional syndrome which has been widely studied in the field of organizational psychology (Maslach et al., 2001). When burnout symptoms are severe enough to cause clinically significant distress and functional impairment, it is referred to as clinical burnout (Grossi et al., 2015; van Dam, 2021). In Sweden, exhaustion disorder (ED) is used in healthcare as a formal diagnosis equivalent to clinical burnout, with physical and psychological exhaustion as the main symptoms (Grossi et al., 2015).

Burnout has been associated with cognitive impairments (Deligkaris et al., 2014), primarily within the domains executive function, working memory, attention and processing speed and episodic memory (Gavelin et al., 2022). Moreover, people with clinical burnout report high levels of mental fatigue during cognitive testing (Krabbe et al., 2017; Oosterholt et al., 2014; Skau et al., 2021; van Dam et al., 2011). However, in this context it is important to distinguish perceptions of mental fatigue from cognitive fatigability, which may be separate and partly independent phenomena (Kluger et al., 2013). Perceptions of mental fatigue refers to the subjective sensation of mental exhaustion, while cognitive fatigability reflects a change in cognitive performance due to fatigue effects (Kluger et al., 2013; Wylie & Flashman, 2017), such as decrements in accuracy or response times (Boksem et al., 2005), or increased intraindividual performance variability over time following prolonged

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cognitive activity (Wang et al., 2014). To date, few studies have addressed the complexity of mental fatigue in clinical burnout and investigated whether perceptions of fatigue is associated with cognitive fatigability.

There are currently no established methods to measure cognitive fatigability in a clinical setting and it can be difficult to distinguish reduced cognitive performance due to an illness or injury from fatigue effects. One way that previous studies have addressed this issue is by using prolonged testing procedures to induce fatigue, often using a test-retest design with the inclusion of a cognitively effortful task, such as a continuous performance test (Krupp & Elkins, 2000; Skau et al., 2019; Skau et al., 2021) or a reading comprehension task (Ashman et al., 2008; Jonasson et al., 2018), between test blocks. Within these designs, cognitive fatigability is commonly manifested as an absence of learning effect in the clinical group as compared to the reference group, i.e., that controls improve their task performance following repeated administration, whereas patients with fatigue do so to a lesser extent (Ashman et al., 2008; Jonasson et al., 2018; Krupp & Elkins, 2000; Skau et al., 2019). This paradigm has also been used in clinical burnout, providing some evidence of cognitive fatigability manifested as slower reaction times in the patient group on an executive function task (Skau et al., 2021). However, the study included former patients who had undergone treatment (time since diagnosis on average 46 months) and a relatively small sample, motivating further investigation into cognitive fatigability in this patient group.

Heart rate variability (HRV) is a non-invasive indicator of autonomic nervous system activity (Shaffer et al., 2014), which is often found to deviate in psychological disorders (Beauchaine & Thayer, 2015). HRV is affected by activity in regulatory brain regions such as the medial prefrontal cortex and amygdala, and is thus regarded as a potential marker for cognitive strain, adaptability and health (Thayer et al., 2012). There are several measures of HRV, including time-domain measures such as the root mean square of successive differences (RMSSD) and the percentage of successive normal sinus R-R intervals more than 50 ms (pNN50), and frequency-domain measures such as high frequency power (HF-HRV). All of these reflect parasympathetic activity or vagal tone and, in turn, adaptive energetic resources, and have been extensively studied in relation to cognition and health (Laborde et al., 2017; Shaffer & Ginsberg, 2017; Shaffer et al., 2014). Lower resting RMSSD has been associated with poorer executive function (Hansen et al., 2003; Stenfors et al., 2016) and reduced cardiovascular reactivity to mental stress in healthy subjects (Weber et al., 2010). Moreover, prolonged cognitive activity has been found to induce increased mental fatigue as well as changes in vagally mediated components of HRV over time (Dallaway et al., 2022; Matuz et al., 2021). In clinical burnout, several HRV measures has been reported as lowered in patients as compared to healthy controls and non-clinical burnout (Lennartsson et al., 2016; Olsson et al., 2010). A study by de Vente et al. (2015) found lower basal RMSSD, but no difference in HRV reactivity to a psychosocial stressor. Conversely, Zanstra et al. (2006) found no differences in resting HF-HRV in individuals with clinical burnout in comparison with controls, but differences in HF-HRV reactivity when performing an inhibition task during a simulated workday. Given the relevance of parasympathetic activity in the context of both cognitive function and mental fatigue, further empirical investigation of autonomic response to sustained mental activity in this patient group is warranted.

The aim of this study was to investigate the effects of sustained mental activity on perceptions of mental fatigue, cognitive performance, and autonomic response in clinical burnout. To this end, patients with clinical burnout and healthy control participants were administered a set of cognitive tests before and after an effortful cognitive task. As a cognitively effortful task, a continuous performance test with concurrent sound exposure was used. The use of sound was based on previous observations that external stressors, such as auditory distraction, is associated with increased mental fatigue even when cognitive performance is unaffected by the distractor (Krabbe et al., 2017). Following the conceptualization of fatigue proposed by Kluger et al. (2013), we sought to investigate fatigue in terms of both perceptions of fatigue and performance fatigability. Perceptions of mental fatigue was assessed through self-ratings of mental fatigue over the course of the test session, and cognitive fatigability was quantified by measuring change in performance on the cognitive tests over time. Finally, HRV was recorded to index autonomic response. We hypothesized that patients with clinical burnout would rate their mental fatigue as higher, show less learning effect on cognitive tasks, and express lower HRV (HF-HRV and RMSSD) than controls when performing tasks requiring sustained mental effort. We further predicted that differences between the groups may increase over time.

2. Methods

2.1. Participants

Patients were recruited from the Stress Rehabilitation Clinic at the University Hospital in Umeå, Sweden. All patients had confirmed diagnosis of ED according to the diagnostic criteria included in the Swedish version of the ICD-10 (code F43.8 A, Table S1). Participants were consecutively recruited from September 2021 to November 2022. All patients referred to the Stress Rehabilitation Clinic for treatment were screened for eligibility by a physician and psychologist working at the clinic. Inclusion criteria for the study were: (1) confirmed diagnosis of ED; (2) age 18–65. The following exclusion criteria were applied: (1) not fluent in Swedish; (2) psychiatric co-morbidity (symptoms of depression or anxiety and/or diagnosis of mixed anxiety and depressive disorder were allowed); (3) other medical condition known to affect cognition, such as cardiovascular or neurological diseases; (4) impaired hearing.

The control group was recruited during the same time period through advertisement on social media and local advertisement boards. Inclusion criteria for the control group was being between 18 and 65 of age. An initial telephone interview was conducted to screen the controls against the same exclusion criteria as the patient group. In addition, controls were excluded if they had a self-reported current or previous history of stress-related or psychiatric disorder (within the past 10 years) or scored $>$ 3.75 on the Shirom-Melamed Burnout Questionnaire (SMBQ) (Grossi et al., 2003) at the time of the study.

A total of 30 patients with clinical burnout and 32 control participants fulfilling the inclusion criteria were recruited to the study. Two control group participants were excluded due to highly elevated error rates on the continuous performance test, as well as clearly observable difficulties during the test session (e.g., low motivation, not complying with task instructions). The study was conducted in accordance with the Declaration of Helsinki and approved by the Swedish Ethical Review Authority (Dnr 2021–01943). All participants provided written informed consent before enrolment and were informed that they could withdraw from the study at any time. A financial compensation of 300 SEK was offered for participation.

2.2. Procedure

The assessments took place at the Department of Psychology at Umeå university and were conducted by a trained clinical psychologist. The sessions lasted for approximately three hours and were conducted between 9.00 a.m. and 12 p.m. for the majority of the participants. Some participants were not able to attend in the morning and therefore conducted the assessment between 1.00 pm and 4 p.m. (four patients and six controls) and 6.00 p.m. and 9 p.m. (one control). Participants were asked to refrain from caffeine, tobacco, and heavy meals the hour before the test session. Before coming to the session, participants filled out questionnaires on demographic variables, psychological well-being, and self-reported executive difficulties.

Fig. 1 shows a schematic overview of the experimental procedure.

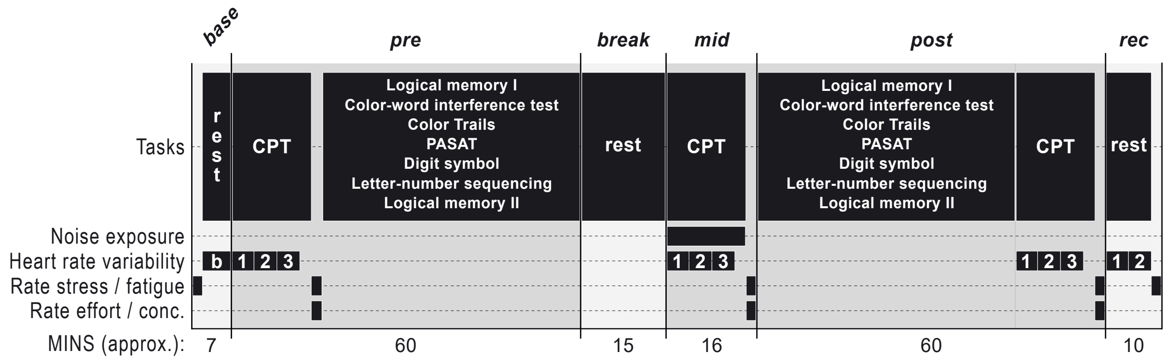

Fig. 1. Overview of the Experimental Procedure. Base = baseline. Conc = concentration difficulties. CPT = Conner's Continuous Performance Test. Mid = middle. Rec = recovery. PASAT = Paced Auditory Serial Addition Test.

The study had a test-retest design in which a cognitive test battery was administered twice (Pre- and Post-test). Each test block lasted 60 min and between the two blocks, a cognitively effortful task was administered as an additional fatigue induction. The test battery included the following tests (see Measures for a more detailed description): (1) Logical memory I; (2) Color-word interference test; (3) Color trails; (4) Paced auditory serial addition test (PASAT); (5) Digit symbol; (6) Letter-number sequencing; (7) Logical memory II; and (8) Conners Continuous performance test (CPT). The order of administration was the same within the two test blocks, with the exception that the CPT was administered as the first task at Pre-test and the last task at Post-test (Fig. 1). The CPT was also administered with concurrent sound exposure as the cognitively effortful task between the two test blocks. Using the CPT as the first and last task of the session as well as for the fatigue induction was chosen to allow for comparisons of ratings of perceived mental fatigue, cognitive performance and HRV parameters in the beginning, middle and end of the test session using the same standardised task.

When participants came to the test session, they were given a general introduction and asked to rate their current level of stress and mental fatigue. Participants were then fitted with electrocardiographic (ECG) electrodes and asked to sit comfortably with their eyes open for five minutes during baseline ECG recording. After this, a first run of the CPT task was performed, followed by the remaining tests in the cognitive test battery (Pre). Subsequently, participants had a 15-min break. The break was included for practical reasons, to ensure that patients could complete the testing procedures. This was followed by the cognitively effortful task, which consisted of a second run of the CPT task with concurrent sound exposure (Mid). During task execution, a sound recording consisting of office noise was played in the background through an iPad (8:th gen) at a sound level of 50 db. The recording was in English, but no specific words or sentences were distinguishable. The stimulus was chosen as a non-semantic potential distractor mimicking everyday noise exposure e.g., at work. Participants then completed the second block of cognitive tests, which finished with a final run of the CPT task (Post). They were then asked to sit comfortably with their eyes open for an 8-min recovery period (Rec). ECG recordings were performed at baseline, during all three administrations of the CPT task and the recovery period. After each run of the CPT task, participants rated their current level of mental fatigue, as well as their perceived level of stress, mental effort, and concentration difficulties during the task. Ratings of current level of stress and mental fatigue were repeated after the recovery period. The questions relating to mental effort and concentration difficulties were included to assess participants' perceptions of the overall demands of the CPT task across the three administrations (i.e., in the beginning, middle and end of the session). The question relating to perceived level of stress was included as a control variable to ensure that participants were not distressed by the test procedures.

2.3. Measures

2.3.1. Cognitive tests

The cognitive test battery consisted of tests assessing executive function, working memory, attention and processing speed and episodic memory, chosen to align with the cognitive domains affected in clinical burnout (Gavelin et al., 2022). When possible, parallel forms were used, and the order of the forms were counterbalanced between the first and second test block.

Inhibition was assessed using the Color-word interference test from the Delis-Kaplan executive function system (Delis et al., 2001). The task was administered according to standardized procedures and the outcome was inhibition cost, calculated as the time taken in seconds to complete incongruent trials as opposed to reading colour words. A higher inhibition cost indicates worse performance.

Shifting was assessed with the Color trails test, using the alternate forms A and B (D'Elia et al., 1996). Participants were asked to connect a series of numbered circles in the correct order, and to do so while also alternating between the colours pink and yellow. A shifting cost was calculated, representing the difference in time taken in seconds to complete the shifting condition compared to the baseline condition. A higher shifting cost implies worse performance.

PASAT was used to assess attention, working memory and processing speed (Gronwall, 1977). In this task, participants listened to a sequence of 61 digits, presented at a rate of 2 s, and were asked to add each presented digit to the previous one. The outcome was the total number of correct responses.

Letter-number-sequencing from the Wechsler Memory Scale III (WMS III) was used to assess working memory (Wechsler, 1997). Participants were presented a series of numbers and letters and asked to recall the numbers in numerical order followed by the letters in alphabetical order. An alternate form was created for this study by using items from the Weschler Adult Intelligence Scale IV. The outcome was total number of correctly recalled sequences.

Digit symbol from the Repeatable Battery for the Assessment of Neuropsychological Status was used to assess processing speed, using the alternate forms A and B (Randolph, 1998). Participants were asked to match as many symbols and digits as possible using a coding key. The outcome was the total number of correctly transcribed items during 90 s.

Logical memory from WMS III was used to assess verbal episodic memory (Wechsler, 1997). Story A and B were used as alternate forms. Each story was presented twice with a free recall after each presentation (Logical Memory I). A delayed free recall was administered approximately 25 min after the first presentation (Logical Memory II). Performance was measured in total number of correctly recalled story units.

The Conners CPT 3 was used to assess attention (Conners, 2014). In this task, letters were presented on a computer screen and participants were instructed to respond as quickly as possible by pressing the space bar for each presented letter, except for the letter "X". The task lasts for

14 min, and three variables were used as outcome measures: (1) hit reaction time, indexing processing speed; (2) hit reaction time standard deviation, indexing response speed consistency and; (3) commissions, indexing response inhibition. Raw scores were transformed into T-scores based on demographically corrected normative values. For all variables, a higher T-score indicates worse performance, i.e., slower response speed, higher inconsistency in reaction times and more commission errors. A composite score was calculated consisting of the mean T-score of the three outcome variables, to reflect overall performance on the task.

2.3.2. Self-report measures

The SMBQ was used to assess level of burnout (Lundgren-Nilsson et al., 2012; Melamed et al., 1992). This instrument consists of 22 items rated on a 7-point Likert scale ranging from 1 (almost never) to 7 (always). The mean score of all items was used, with higher score indicating higher level of burnout. Cronbach's alpha for this measure was 0.98.

The Hospital Anxiety and Depression Scale was used to assess level of depression and anxiety (Zigmond & Snaith, 1983). The questionnaire consists of 14 items rated on a 4-point Likert scale (0−3). The total score for each subscale was calculated as the sum of the seven items targeting depression and anxiety, respectively (range 0–21). Cronbach's alpha was 0.90 for both the depression and the anxiety subscale.

The Behavior Rating Inventory of Executive Function – Adult Version was used to asses self-reported executive difficulties (Roth et al., 2005). The questionnaire consists of a 75-item list of behaviours and the respondent is asked to rate how often each behaviour was a problem for them over the past month (never, sometimes, or often). Raw scores were transformed to T-scores based on normative values adjusted for age, with a clinically elevated score defined as T-score > 65 (Roth et al., 2005). Cronbach's alpha was 0.97.

The Mental Fatigue Scale was used to assess mental fatigue over the past month (Johansson et al., 2009). The scale consists of 14 items rated on a scale from 0 to 3 and covers different aspects of fatigue (e.g., lack of initiative, mental recovery, concentration difficulties, sensitivity to noise). The sum score of all items was computed, with a higher score indicating more mental fatigue. Cronbach's alpha was 0.96.

A Borg CR-100 scale (Borg & Borg, 2002) was used to assess perceived level of mental fatigue, task demands (mental effort and concentration difficulties) and stress continuously during the test session. The scale is a verbally anchored ratio scale with adjectives corresponding to numbers on the scale: None = 0; Minimal = 2; Extremely weak = 3; Very weak = 5; Weak = 13; Moderate = 25; Fairly strong = 37; Strong = 50; Very strong = 70; Extremely strong = 90; Almost maximal = 100. The scale extends to 120, but without a descriptive adjective.

2.3.3. Heart rate variability

ECG were collected at a sampling rate of 200 Hz through disposable electrodes (EL503) attached to the non-dominant wrist and corresponding ankle using a Biopac MP150 system. R-peak detection, editing of R-R intervals and calculation of HRV was done using Kubios 2.1 (Kubios OY). The ECG:s were visually inspected for artefacts, which were manually corrected and removed if necessary, followed by the very low artefact correction option of the Kubios software. Analyses were made using the high-frequency (0.15 – 0.4 Hz) power band HRV (HF-HRV) and RMSSD, indexing parasympathetic or vagal activity in the frequency and time domain, respectively (Shaffer et al., 2014). The calculations of HRV parameters were done in 4-min intervals. For the 5-min baseline recording, the first 60 s were considered an adaptation period and the subsequent four minutes were used in the analysis. Each run of the CPT task lasted for 14 min, of which the first 12 min of the ECG recording was used for the analysis, divided into three 4-min intervals. The 8-min recovery recording was split into two 4-min intervals.

2.4. Statistical analysis

Statistical analyses were performed in R. For demographic and background characteristics, differences between the groups were analysed using independent samples *t*-tests for continuous variables and Pearson's Chi-square tests for categorical variables. To investigate changes in perceived mental fatigue, cognitive performance, and HRV, we used multilevel modelling, specifically a linear mixed-effects model fitted with restricted maximum likelihood estimation using the nlme package (Pinheiro et al., 2022). The models included time, group and the interaction between time and group as fixed effects and a random intercept for each participant. Time was included as a categorical variable. The models included two time points (Pre and Post) for the cognitive tests; three time points (Pre, Mid and Post) for the CPT task and ratings of mental effort and concentration difficulties; and five time points (Baseline, Pre, Mid, Post and Rec) for the HRV parameters and mental fatigue ratings. For each fitted model, the statistical significance of the overall Group x Time interaction term was tested with analysis of variance. Significant interaction effects were followed by pairwise comparisons of the change across time within each group based on the estimated marginal means of the model, using the emmeans package (Lenth, 2022), with Holm correction for multiple comparisons. Cohen's *d* was calculated as the mean difference between the groups at each time-point divided by the pooled standard deviation using the package effectsize (Ben-Shachar et al., 2020).

Model assumptions were checked by visually inspecting the data and the standardized residuals, and by plotting fitted values versus standardized residuals. The HRV parameters, CPT Composite and Inhibition cost were log-transformed to improve normality and reduce the influence of outliers (Tabachnick & Fidell, 2014). The statistical analyses for these variables were subsequently conducted based on transformed scores. For descriptive purposes, the non-transformed scores of the CPT Composite and Inhibition cost are presented.

3. Results

3.1. Sample characteristics

Demographic and clinical characteristics of the sample are shown in Table 1. The groups were similar in age and education level but there was a slightly larger proportion of men in the control group. Full-time sick-leave was reported by 13% of the patients, 57% reported part-time sick-leave and 30% reported no sick-leave. Self-reported time since ED diagnosis ranged between 1 and 120 months, with the majority of participants (63%) being diagnosed within the past 12 months. Antidepressant use was reported by 47% of the patients and 10% of the controls. The patient group showed significantly higher symptoms of burnout, depression, anxiety, and mental fatigue and reported more executive difficulties in everyday life compared to controls.

3.2. Perceptions of mental fatigue

Fig. 2 shows ratings of mental fatigue across the test session. There was a significant Group x Time interaction effect for perceived mental fatigue, $F(4, 232) = 5.18$, $p < .001$. *Post hoc* tests showed that mental fatigue increased significantly for the clinical burnout group across all measurement points from Baseline to Post (all p's $< .01$), whereas no significant change was seen between Post and Rec ($p = .33$). For the control group, mental fatigue increased significantly from Pre to Mid ($p = .003$) and Mid to Post ($p = .036$) and then decreased from Post to Rec ($p = .012$). As a control analysis, ratings of perceived stress across the test session were also investigated. No significant Group x Time interaction was found, $F(4, 232) = 0.86$, $p = .49$. A graphical overview of the ratings of perceived stress across the test session can be found in Fig. S1.

Table 1
Sample Characteristics.

Variable		Clinical burnout $n = 30$	Control $n = 30$	*p*-value
Age		42.53 (7.63)	41.17 (13.40)	.63[a]
Gender, n (%)	Women	28 (93%)	21 (70%)	.061[b]
	Men	2 (7%)	8 (27%)	
	Non-binary	0 (0%)	1 (3%)	
Education, n (%)	Elementary school	1 (3%)	0 (0%)	.46[b]
	High school	9 (30%)	12 (40%)	
	University	20 (67%)	18 (60%)	
Sick-leave, n (%)	100%	4 (13%)	0 (0%)	
	75%	2 (7%)	0 (0%)	
	50%	12 (40%)	0 (0%)	
	25%	3 (10%)	0 (0%)	
	0%	9 (30%)	30 (100%)	
Months since ED diagnosis, median (range)		7.5 (1 – 120)	na	
Antidepressant use, n (%)		14 (47%)	3 (10%)	.004[b]
SMBQ burnout		4.87 (0.93)	2.14 (0.66)	< .001[a]
HADS depression		7.83 (3.76)	2.00 (2.39)	< .001[a]
HADS anxiety		9.37 (5.42)	4.17 (3.29)	< .001[a]
Mental Fatigue Scale		20.87 (4.26)	4.68 (4.31)	< .001[a]
BRIEF Global Executive Composite		61.47 (11.01)	44.60 (7.48)	< .001[a]

Note. Values are presented as mean (standard deviation) unless otherwise indicated. na = not applicable. BRIEF = Behavior Rating Inventory of Executive Function – Adult Version. HADS = Hospital Anxiety and Depression Scale. SMBQ = Shirom-Melamed Burnout Questionnaire.
[a] Based on Independent samples *t*-test
[b] Based on Pearson's Chi-square test

3.3. Cognitive performance and ratings of task demands

There was a significant Group x Time interaction effect for Inhibition cost and PASAT (Table 2). *Post hoc* tests showed that the control group improved their performance from Pre to Post on both tasks (p's < .001), whereas the clinical burnout group's performance did not change significantly across time (both p's = .11). There was no significant difference in change across time between the groups for Shift cost, Digit symbol, Letter-number sequencing, or Logical memory.

Fig. 3 displays performance on the CPT Composite and associated ratings of Mental effort and Concentration difficulties across the test session. Group means and standard deviations for the CPT Composite and each of the performance outcome variables, as well as ratings of Mental effort and Concentration difficulties are shown in Table S2. There was a significant Group x Time interaction effect for the CPT Composite, $F(2, 116) = 3.22$, $p = .044$. *Post hoc* tests showed that the control group's performance improved from Pre to Mid ($p = .041$), whereas no significant change was seen from Mid to Post ($p = .61$). There was no significant change in performance across time for the clinical burnout group (p's > .40). For ratings of task demands, there was a significant Group x Time interaction effect for Concentration difficulties, $F(2, 116) = 3.75$, $p = .027$. *Post hoc* tests showed that for the clinical burnout group, ratings of concentration difficulties increased from Pre to Mid ($p < .001$) and from Mid to Post ($p = .009$). For the control group, there was no significant change between Pre and Mid ($p = .087$), followed by a significant increase in concentration difficulties from Mid to Post ($p = .023$). No significant Group x Time interaction effect was seen for ratings of Mental effort, $F(2, 116) = 2.61$, $p = .078$).

3.4. Heart rate variability

One control participant was excluded from the analysis of HRV, and one only provided baseline data, due to measurement difficulties. Visual inspection of the log-transformed data revealed one outlier in the clinical burnout group with very low baseline HRV. Since the participant was on tricyclic antidepressant medication, which has been associated with reduced HRV (Alvares et al., 2016), he/she was excluded from the analysis. The results from the analysis including this participant can be found in Fig. S2.

A graphical overview of the HRV parameters across the test session is shown in Fig. 4. There was no difference in HF-HRV or RMSSD between the groups at baseline ($p = .55$ and $p = .64$, respectively). There was a significant Group x Time interaction effect for HF-HRV, $F(4, 617) = 2.83$, $p = .024$. *Post hoc* tests showed that for both groups, HF-HRV increased from Pre to Mid ($p < .001$). There was a unique decrease in

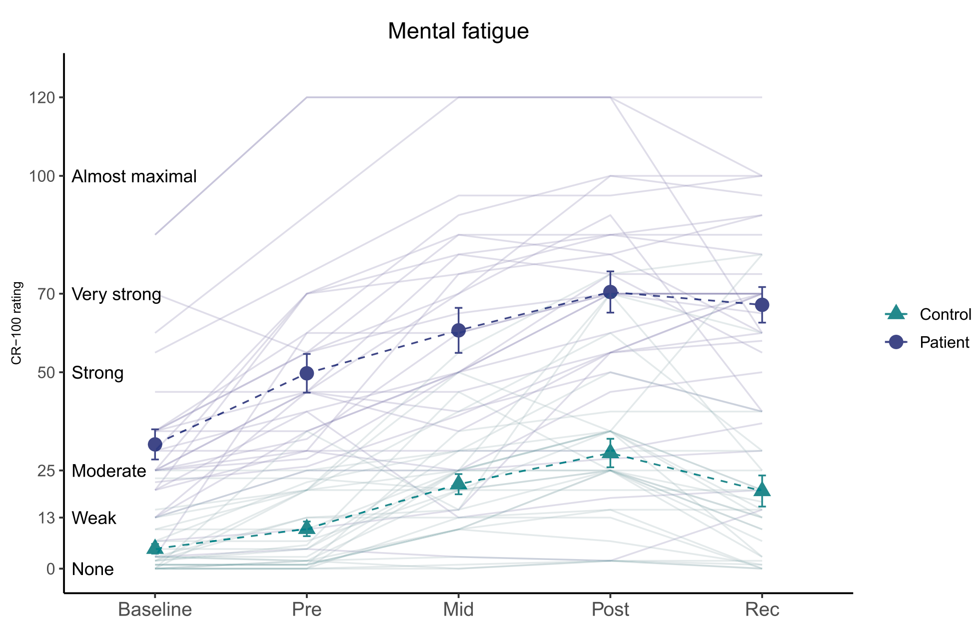

Fig. 2. Ratings of Mental Fatigue Across the Test Session. Error bars indicate SEM. Mid = middle. Rec = recovery.

Table 2
Cognitive Test Performance.

Variable	Clinical burnout $n = 30$	Control $n = 30$	Cohen's d (95% CI)	Statistics Group x Time
Inhibition cost				$F(1, 58)= 4.60$, $p = .036$[a]
Pre	26.80 (9.22)	27.27 (8.71)	0.05 (−0.45 to 0.56)	
Post	25.37 (10.31)	22.70 (7.91)	-0.29 (−0.80 to 0.22)	
Shift cost				$F(1, 57)= 0.04$, $p = .84$
Pre	35.20 (12.23)	38.17 (15.39)[b]	0.21 (−0.30 to 0.73)	
Post	30.60 (9.32)	32.70 (12.82)[b]	0.19 (−0.33 to 0.70)	
PASAT				$F(1, 58)= 4.25$, $p = .044$
Pre	44.13 (8.45)	45.77 (10.05)	-0.18 (−0.68 to 0.33)	
Post	45.57 (8.63)	49.80 (7.43)	-0.53 (−1.04 to −0.01)	
Digit symbol				$F(1, 58)= 2.23$, $p = .14$
Pre	55.67 (9.19)	54.67 (6.06)	0.13 (−0.38 to 0.63)	
Post	54.13 (7.95)	55.37 (7.27)	-0.16 (−0.67 to 0.35)	
Letter-number sequencing				$F(1, 58)= 0.005$, $p = .95$
Pre	10.67 (2.04)	11.67 (2.09)	-0.48 (−1.00 to 0.04)	
Post	10.97 (2.17)	11.93 (2.45)	-0.42 (−0.93 to 0.10)	
Logical memory immediate				$F(1, 58)= 0.51$, $p = .48$
Pre	32.80 (5.86)	34.67 (6.83)	-0.29 (−0.80 to 0.22)	
Post	35.07 (6.21)	35.47 (6.85)	-0.06 (−0.57 to 0.45)	
Logical memory delayed				$F(1, 58)= 0.08$, $p = .78$
Pre	18.47 (3.06)	18.77 (3.86)	-0.09 (−0.59 to 0.42)	
Post	18.63 (3.16)	19.20 (3.33)	-0.17 (−0.68 to 0.33)	

Note. Values are presented as mean (standard deviation). p-values are from mixed-effects models with a random intercept for each participant comparing difference in change between the groups. A negative effect size indicates worse performance in the clinical burnout group. CI = confidence interval. PASAT = Paced auditory serial addition test.
[a] Based on log-transformed scores
[b] $n = 29$

HF-HRV from Mid to Post in the clinical burnout group ($p = .013$), whereas no significant change was seen for the control group ($p = .74$). A statistically significant Group x Time interaction effect was also found for RMSSD, $F(4, 617) = 2.98$, $p = .019$. *Post hoc* tests showed that for the control group, RMSSD increased from Baseline to Pre ($p = .010$) and Pre to Mid ($p < .001$). For the clinical burnout group, RMSSD increased from Pre to Mid ($p < .001$) and then decreased from Mid to Post, although this effect did not remain statistically significant after adjustment for multiple comparisons (Holm-adjusted $p = .058$, non-adjusted $p = .019$). The Group x Time interactions remained significant after including age, gender, antidepressant medication and time of the assessment (morning or afternoon) as covariates.

4. Discussion

The aim of this study was to investigate the effects of sustained mental activity on perceptions of mental fatigue, cognitive performance, and autonomic response in clinical burnout. We found that, in comparison with controls, the levels of mental fatigue in the clinical burnout group increased earlier in the session and did not recover following the 8-min rest period. Moreover, the patient group showed less improvement on some of the cognitive tests, mainly those involving attention and processing speed, inhibition and working memory. The groups differed in their autonomic response and this difference became evident by the end of the 3-hour test session.

The results from this study align with previous findings that people with clinical burnout report high levels of mental fatigue when performing cognitive tasks (Krabbe et al., 2017; Oosterholt et al., 2014; Skau et al., 2021; van Dam et al., 2011). Here, we extend those findings by investigating the time course of changes in mental fatigue during sustained mental activity in more detail. Our results showed that for the clinical burnout group, levels of mental fatigue were high at baseline and increased already after the first run of the 15-min CPT task, which was the first task administered in the session. Moreover, their levels of mental fatigue remained high after the recovery period. In contrast, the control group reported increased levels of mental fatigue in the middle and end of the test session and a decrease after the recovery period. Thus, for perceptions of mental fatigue, patients responded faster and did not recover, while controls showed a more flexible response, characterized by a gradual increase and a decrease following a short rest period. Notably, the increase in mental fatigue across the middle and end of the test session was similar for both groups, suggesting that group differences in change across time were primarily due to differences in initial response and recovery.

Differences in change across time were found for some, but not all, of the cognitive tests. Specifically, group differences were found for Inhibition cost, PASAT and the CPT task, showing that the control group became more proficient with these tasks following repeated administration, whereas the patient group showed no improvement across time. Overall, these tasks require attention and processing speed, inhibition and working memory. Interestingly, no difference was found for Letter-number sequencing, which requires working memory but places lesser demands on processing speed. Taken together, the pattern of findings suggests that tasks with simultaneous demands on attention, processing speed and executive functions/working memory are the most susceptible to cognitive fatigability in this patient group. This aligns with the proposition that cognitive fatigability mainly affects three cognitive domains: attention, executive function and psychomotor speed (Wylie & Flashman, 2017), and in particular tasks requiring simultaneous processing of these cognitive functions (Möller et al., 2014), as well as with observations that mental fatigue is associated with longer reaction times on executive function tasks in clinical burnout (Skau et al., 2021; van Dam et al., 2011).

The ratings of task demands indicated that patients struggled with maintaining their concentration during the CPT task, which became increasingly difficult across the session, and that performing the task required substantial mental effort. To interpret these findings, it may be useful to distinguish between performance effectiveness, i.e., the quality of task performance, and processing efficiency, i.e., the effort or resources spent to achieve a certain level of performance (Eysenck et al., 2007; Hockey, 1997). Following this conceptualisation, the pattern of performance on the CPT task and associated self-ratings may indicate that patients showed decreased efficiency across time, i.e., that more self-perceived resources were required to maintain task performance. In contrast, the control group showed improved task performance over time, albeit with progressively increasing self-perceived costs. This could indicate that the performance-effort balance was affected by sustained mental activity for both groups, but that these effects were more pronounced for individuals with clinical burnout. The pattern of findings is similar to a previous study by Zanstra et al. (2006), who found that healthy controls improved their performance levels on a Stroop task during a simulated workday, whereas the clinical burnout group's performance did not improve, in conjunction with more effort

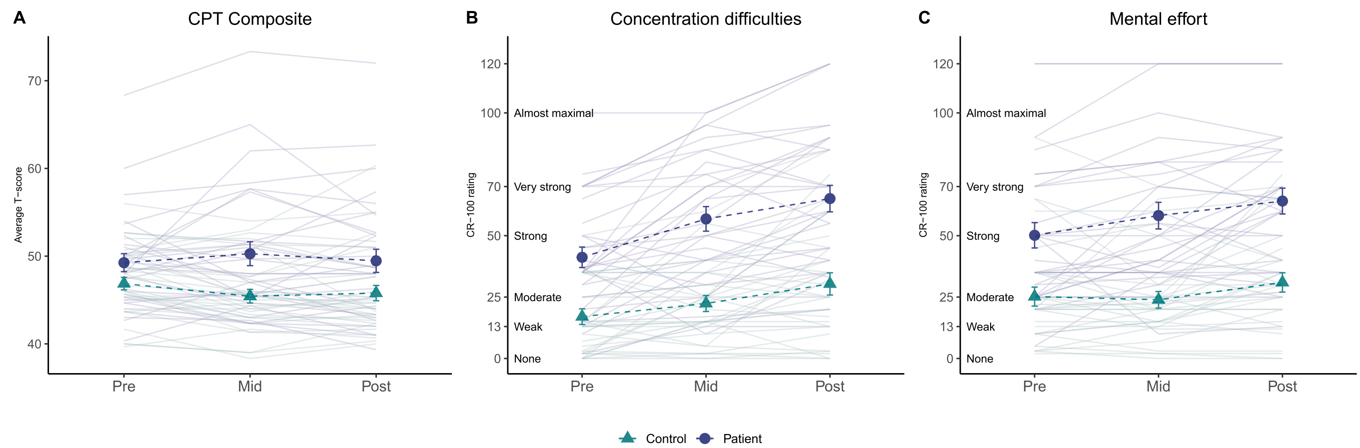

Fig. 3. Performance on (A) the CPT Composite and Ratings of (B) Concentration Difficulties and (C) Mental Effort Across the Test Session. Error bars indicate SEM. CPT = Conners Continuous Performance Test. Mid = middle.

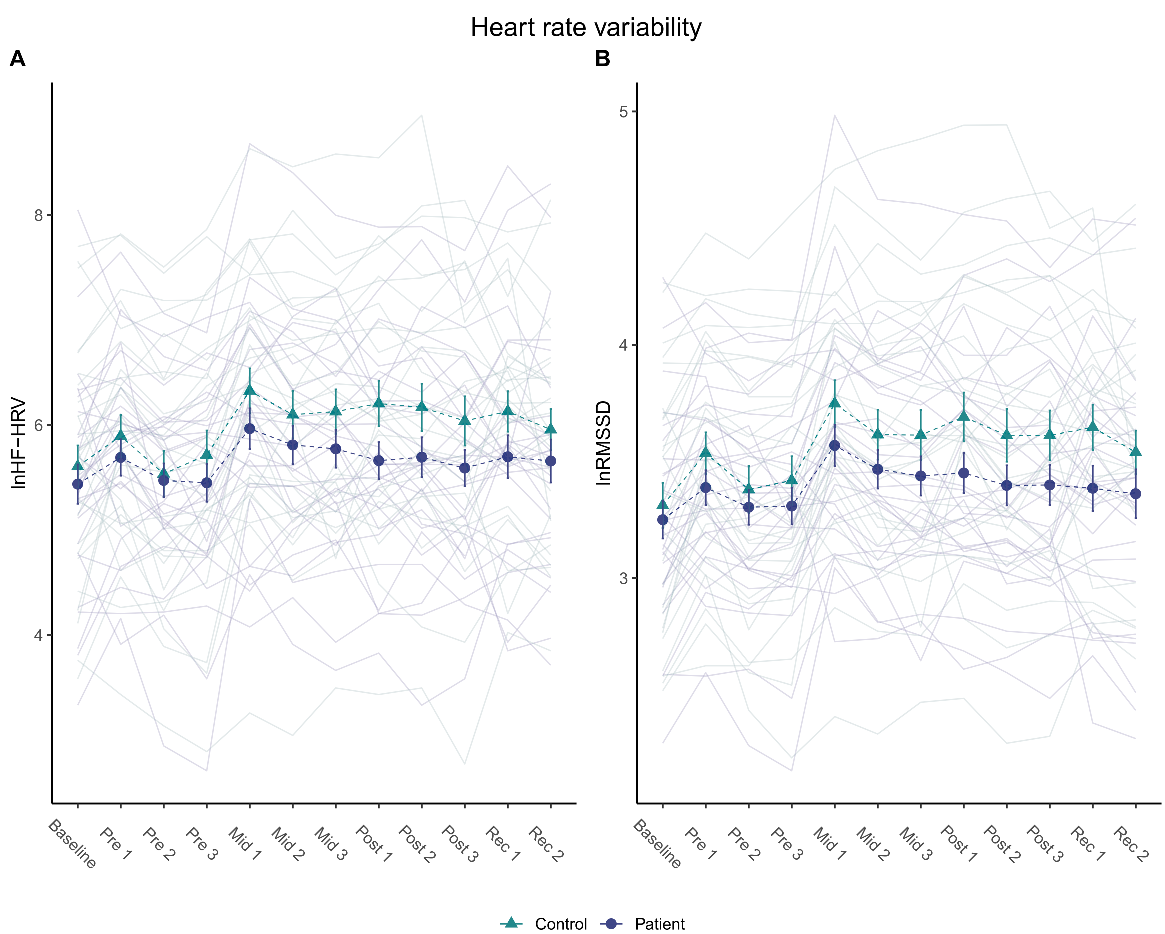

Fig. 4. Change in (A) HF-HRV and (B) RMSSD Across the Test Session. The figure displays the means of each 4-min phase. Error bars represent SEM. lnHF-HRV = log-transformed high-frequency heart rate variability. lnRMSSD = log-transformed root mean square of successive differences. Mid = middle. Rec = recovery.

invested in the task as the day progressed. While we did not find evidence that the sound exposure adversely affected patients' performance on the CPT task, it should be noted that the effect sizes for group differences in task performance and associated self-ratings were largest during the second administration of the task (see Table S2). Thus, further investigation of the effects of noise and other potentially disrupting stimuli in clinical burnout is warranted.

We found no differences between the groups in HRV (HF-HRV or RMSSD) at baseline; instead, a significant difference in change across time emerged. Notably, similar changes were seen between the first and second run of the CPT task, in which HF-HRV and RMSSD increased for both groups. A possible explanation for this increase could be the 15-min break before the second administration. The groups instead differed in their change in autonomic response between the second and third administration of the CPT; specifically, the clinical burnout group's HRV decreased, reaching statistical significance for HF-HRV but not for RMSSD after correction for multiple comparisons, whereas no change was seen for the control group. While both an increase and a decrease in vagally mediated components of HRV can be seen as adaptive depending on the situation and task demands (Laborde et al., 2018), lower HRV in response to cognitive performance is thought to indicate mental effort (Mandrick et al., 2016) and demands of sustained attention (Luque-Casado et al., 2016), whereas an increase in HRV following time-on-task has been interpreted as indicative of task familiarization (Dallaway et al., 2022) or disengagement (Matuz et al., 2021). Thus, our findings may suggest that controls adapt to the task, such that it requires less effort as time progresses, while patients do so to a lesser extent and instead continue to respond with more effort expenditure at later stages of the session. Importantly, this difference did not become evident until the final part of the 3-hour session.

The HRV results are thus interesting as they suggest group differences during task engagement, but not during baseline. We nevertheless endorse a cautionary stance when speculating about the cause of these differences. Although the HRV measures used in this study have been associated with fluctuations in vagal tone (Laborde et al., 2017), we acknowledge that several other regulatory systems could have affected the outcomes. For instance, as pointed out during the review process of the manuscript, fluctuations in heart rate are intrinsically affected by breathing patterns, but not always in a constant fashion (see e.g., Grossman & Taylor, 2007). Rapid and shallow breathing will in general decrease respiratory sinus arrhythmia, and slow, deep breathing will increase it, which alters HRV measures. Intermittent changes in breathing, such as sighs or yawns, may also impact HRV parameters, and such respiratory behaviours are also associated with executive demands (Quintana et al., 2016). Some patient groups consistently express deviating breathing patterns. Such results have, for instance, been observed in conditions such as panic disorder (Meuret et al., 2018). In a similar vein, paced breathing exercises results in both increased HRV and decreased symptoms in patients with panic disorder (Herhaus et al., 2022). The HRV results in the current study may thus be influenced by baseline or transient differences in breathing between the groups, or a combination of both.

We opted to omit respiratory monitoring in the current study, with the rationale that additional measurement instruments might affect the patient and control group unequally (e.g., by serving as a distractor for the patient group during the cognitive testing). We nevertheless acknowledge that this disallows us form making more in-depth analyses of how respiration may have influenced HRV results. Hence, we regard current results as a hint of a regulatory imbalance in clinical burnout without speculating further into the root cause of this effect. Including respiration would be important in future studies, but arguably also other autonomic measures such as electrodermal activity, which has been found to deviate in a variety of psychiatric conditions (Vahey & Becerra, 2015). Perhaps even more pertinent, the lower HRV during strenuous cognitive tasks, in combination with worse performance on tasks that requires inhibition, may hint at an even more encompassing imbalance that could involve key inhibitory / saliency regions of the brain, such as the rostral anterior cingulate and anterior insula. These areas are argued to be involved in the regulation of diverse but for this topic pertinent domains such as cognition, heart-rate variability, and disordered breathing (Rosenkranz & Davidson, 2009; Thayer et al., 2009) and areas of further study based on the current results would be to investigate deviations in these regions in clinical burnout using brain imaging methods. Nevertheless, for the purpose of this study, we suggest that the HRV results are interesting as they reveal a situational deviation in an important measure of strain, but that they should be regarded as an important and unique basis for future studies.

Overall, the pattern of findings in this study is consistent with the high-effort approach proposed in clinical burnout (Krabbe et al., 2017; Oosterholt et al., 2014), with effort being reflected by self-ratings as well as HRV response. While we did not find evidence for a performance decline within the patient group across time, it seems plausible that the absence of learning effects within the test-retest design may translate into impaired cognitive performance in an everyday context. Subtle deficits in attention, executive function and working memory following sustained mental activity provides a possible explanation for the cognitive difficulties patients describe in everyday life, which can be difficult to capture through traditional neuropsychological tests (Nelson et al., 2021). Administering tasks that are susceptible to fatigue effects when patients are more tired (e.g., at the end of neuropsychological testing or after a workday) could be one way to assess cognitive fatigability in a clinical setting. From a clinical perspective, the high-effort approach has been conceptualized as a form of maladaptive coping, in which the individual responds to stressful situations with perseverance, rather than engaging in more adaptive self-regulation (Bakker & de Vries, 2021; van Dam, 2021), such as adjusting the current behavioural strategy in response to perceptions of fatigue (Boksem & Tops, 2008). This could lead to a vicious circle that maintains or aggravates symptoms of exhaustion; however, this warrants further investigation.

Some limitations of this study should be addressed. Although we strived to match the patient group and control group on relevant background variables, there was a slightly larger proportion of men in the control group. However, controlling for gender in the analyses did not change the results (data not shown). Moreover, some patients declined participation due to the long testing procedure. Thus, the study sample may not be fully representative of the patient population, as those with the most pronounced difficulties with fatigue may have declined to participate. Nevertheless, a strength of the study is the stringent recruitment procedure in a clinical setting, ensuring that all patients had a confirmed diagnosis of ED and were recruited during the same time frame (i.e., before starting stress rehabilitation). Moreover, the prolonged testing procedure and sound exposure used in the current study may induce not only fatigue but also stress. However, although the clinical burnout group reported moderate stress levels during the session, the pattern of change in perceived stress across time was similar for both groups, making the observed differences in change in cognitive performance and HRV across time less likely to be due to stress exposure. A final limitation is that we did not control for sleep or respiration in our analyses, as these factors may influence HRV (Laborde et al., 2017). The best approach for monitoring and controlling for respiration is debated (see Quintana & Heathers, 2014 for a review) and while RMSSD is less influenced by respiration than HF-HRV (Laborde et al., 2017), respiratory effects are a potential confounder in our findings that should be considered in future research. In light of these limitations and the relatively small sample size, these initial findings need to be interpreted with caution and confirmed in larger studies, and longitudinal investigations are warranted to explore temporal associations between parasympathetic regulation and cognitive symptoms in burnout.

5. Conclusions

To conclude, the results from this study show that patients with clinical burnout are affected differently than controls by sustained mental activity. This was seen in ratings of perceived mental fatigue, autonomic response, and performance on cognitive tasks involving simultaneous demands on attention and processing speed and executive function/working memory. While differences in perceived mental fatigue were evident early in the session, differences in autonomic response emerged at the end of the 3-hour session. These findings highlight the importance of considering mental fatigue and its relation to cognitive performance in clinical burnout. Given that HRV is viewed as a marker of cognitive and affective regulation and adaptation to stressors (Mulcahy et al., 2019; Perna et al., 2020), our findings motivate further research on the role of autonomic dysfunction in relation to cognitive function, as well as the broader symptomology in clinical burnout.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors did not use generative AI technologies for preparation of this work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.biopsycho.2023.108661.

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