Accepted Manuscript

Autonomic nervous system function, activity patterns, and sleep after physical or cognitive challenge in people with chronic fatigue syndrome

Erin Cvejic, Carolina X. Sandler, Andrew Keech, Benjamin K. Barry, Andrew R. Lloyd, Uté Vollmer-Conna

PII: S0022-3999(17)30498-1
DOI: doi:10.1016/j.jpsychores.2017.10.010
Reference: PSR 9425

To appear in: *Journal of Psychosomatic Research*

Received date: 1 June 2017
Revised date: 25 September 2017
Accepted date: 19 October 2017

Please cite this article as: Erin Cvejic, Carolina X. Sandler, Andrew Keech, Benjamin K. Barry, Andrew R. Lloyd, Uté Vollmer-Conna , Autonomic nervous system function, activity patterns, and sleep after physical or cognitive challenge in people with chronic fatigue syndrome. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Psr(2017), doi:10.1016/j.jpsychores.2017.10.010

Autonomic nervous system function, activity patterns, and sleep after physical or cognitive challenge in people with chronic fatigue syndrome

Erin Cvejic, PhD[1,2^], Carolina X. Sandler, PhD[3], Andrew Keech, PhD[4], Benjamin K. Barry, PhD[4,5], Andrew R. Lloyd, MD[3,6], Uté Vollmer-Conna, PhD[1*]

[1] School of Psychiatry, University of New South Wales, NSW Australia, [2] University of Sydney, School of Public Health, NSW Australia, [3] UNSW Fatigue Clinic, University of New South Wales, NSW Australia, [4] School of Medical Sciences, University of New South Wales, NSW Australia, [5] Neuroscience Research Australia, NSW Australia, [6] Viral Immunology Systems Program, The Kirby Institute, University of New South Wales, NSW Australia.

RUNNING HEAD: Post-exertional autonomic functioning in chronic fatigue

Submitted to: Journal of Psychosomatic Research

Submission format: Short Communication

^ *Submission correspondence. Address*:

Dr Erin Cvejic

Sydney School of Public Health, Sydney Medical School

Level 3, Edward Ford Building (A27), University of Sydney, NSW AUSTRALIA 2006

E: erin.cvejic@sydney.edu.au || Ph: +61 2 9351 5305

* *Correspondence upon publication. Address:*

A/Prof Uté Vollmer-Conna

Department of Human Behaviour, School of Psychiatry

Level 1, 30 Botany Street, UNSW SYDNEY, NSW AUSTRALIA 2052

E: ute@unsw.edu.au || Ph: +61 2 9385 2945

Author email addresses: erin.cvejic@sydney.edu.au (EC); c.sandler@unsw.edu.au (CXS); a.keech@unsw.edu.au (AK); ben.barry@unsw.edu.au (BKB); a.lloyd@unsw.edu.au (ARL); ute@unsw.edu.au (UVC)

Abstract

Objective: To explore changes in autonomic functioning, sleep, and physical activity during a post-exertional symptom exacerbation induced by physical or cognitive challenge in participants with chronic fatigue syndrome (CFS).

Methods: Thirty-five participants with CFS reported fatigue levels 24-hours before, immediately before, immediately after, and 24-hours after the completion of previously characterised physical (stationary cycling) or cognitive (simulated driving) challenges. Participants also provided ratings of their sleep quality and sleep duration for the night before, and after, the challenge. Continuous ambulatory electrocardiography (ECG) and physical activity was recorded from 24-hours prior, until 24-hours after, the challenge. Heart rate (HR) and HR variability (HRV, as high frequency power in normalized units) was derived from the ECG trace for periods of wake and sleep.

Results: Both physical and cognitive challenges induced an immediate exacerbation of the fatigue state ($p<0.001$), which remained elevated 24-hours post-challenge. After completing the challenges, participants spent a greater proportion of wakeful hours lying down ($p=0.024$), but did not experience significant changes in sleep quality or sleep duration. Although the normal changes in HR and HRV during the transition from wakefulness to sleep were evident, the magnitude of the increase in HRV was significantly lower after completing the challenge ($p=0.016$).

Conclusion: Preliminary evidence of reduced nocturnal parasympathetic activity, and increased periods of inactivity, were found during post-exertional fatigue in a well-defined group of participants with CFS. Larger studies employing challenge paradigms are warranted to further explore the underlying pathophysiological mechanisms of post-exertional fatigue in CFS.

KEYWORDS

chronic fatigue syndrome; post-exertional fatigue; heart rate variability; parasympathetic; sleep.

1. Introduction

Chronic fatigue syndrome (CFS) is a debilitating disorder of unknown pathogenesis, characterised by fatigue which is not relieved by rest, and is accompanied by constitutional symptoms including cognitive difficulties and unrefreshing sleep [1]. Transient exacerbation of the fatigue state after relatively minor activity (termed 'post-exertional fatigue') constitutes a hallmark symptom of CFS, a phenomenon previously documented in a controlled laboratory setting following both physical and cognitive challenges [2-4]. Fatigue levels rise after challenge, and remain elevated for a prolonged period, taking hours to days to return back to baseline levels. The pathophysiological processes underlying this post-exertional symptom exacerbation remain unclear.

Altered autonomic nervous system (ANS) functioning has been frequently reported in patients with CFS [5, 6], and other disorders featuring fatigue and pain [7-10]. Heart rate variability (HRV), a measure of heart inter-beat interval fluctuations, provides an index of the relative activity of the sympathetic and parasympathetic divisions of the ANS [11]. Changes in HRV are observed in healthy participants after performing fatigue-inducing, sustained mental and physical challenges [12-14], but has not been systematically explored in individuals with CFS during the post-exertional worsening of symptoms. Additionally, ANS imbalance impacts on sleep physiology and quality [15], with preliminary evidence suggesting that reduced HRV in patients with CFS is most prominent during sleep [16, 17]. Thus, it is plausible that nocturnal HRV alterations following day-to-day challenges may contribute to the pathophysiology of the fatigue state.

In this exploratory study, we examined autonomic balance, and changes in sleep / activity behaviour, during the exacerbation of fatigue induced by physical and cognitive challenges in a well-characterised sample of participants with CFS. We hypothesised that the post-exertional fatigue experienced by participants with CFS following physical and cognitive challenges would be accompanied by reduced HRV, more sleep, and reduced activity.

2. Methods

2.1. Design and sample

A within-subjects, repeated-measures design was employed. Participants reported fatigue levels: 24-hours prior and again immediately prior to (averaged to represent baseline), immediately after, and 24-hours after, physical or cognitive challenge. Continuous ambulatory electrocardiography (ECG) and physical activity was recorded from 24-hours prior to 24-hours after challenge. Full details of the challenge protocols have previously been reported [2]. Briefly, participants completed either a moderate-intensity aerobic exercise (PHYS; 25-minutes stationary cycling with workload equivalent to 70% age-predicted maximal heart rate) or a cognitively-demanding challenge (COG; 30-minutes of simulated driving adhering to road rules). All participants were assessed between 11.00AM and 2.00PM under controlled laboratory conditions. Protocols were approved by the institutional human research ethics committee. All participants provided informed, written consent prior to participating.

Thirty-five participants with a primary diagnosis of CFS (according to international diagnostic criteria [1]) were recruited from a specialised tertiary referral clinic providing an outpatient management program for CFS [18]. Participants were approached after their treating clinicians had resolved that they had a stable pattern of symptoms (i.e., consistently endorsed the same symptoms without major fluctuations in severity) as well as optimised sleep-wake cycle (i.e., regimented night-time sleep routine with consistent sleep and rise times, and minimised daytime napping) and mood profiles. Medications affecting autonomic functioning (including beta-blockers, corticosteroids, and benzodiazepines), or any other contraindication to participation (e.g., untreated anxiety, uncontrolled cardiovascular complaints) were exclusionary. For the PHYS challenge (n=24), participants were eligible if they were completing clinician-prescribed regular low-intensity exercise (e.g., 10-minutes of gentle pace walking) without symptom exacerbation, and were physically capable of performing moderate-intensity aerobic exercise for at least 25 minutes. For the COG challenge (n=11), participants were eligible if they reported experiencing significant cognitive symptoms and a history of worsened symptoms following cognitive activity, knew how to drive a car, and were able to tolerate computer-based tasks for at least 30 minutes.

2.2. Instruments

2.2.1. Self-reported measures

Self-reported fatigue was assessed using the Fatigue and Energy Scale (FES) [2], which records current fatigue severity (i.e. "right now") across physical and mental dimensions using a descriptor-anchored Likert scale ranging from 0 to 10 (e.g. 0 = "no fatigue"; 10 = "absolute maximum fatigue"). Baseline somatic symptoms were recorded using the validated 6-item SOMA subscale [19] of the Somatic and Psychological Health Report (SPHERE) [20]. Sleep quality over the preceding month was assessed using the Pittsburgh Sleep Quality Index (PSQI) [21]; for subsequent assessment of each night's sleep quality, an 11-point Likert scale was utilised.

2.2.2. Autonomic and activity parameters

Ambulatory ECG (256Hz sampling) and movement (via tri-axial accelerometer, 25.6Hz sampling) were recorded via lightweight Equivital EQ-02 module (Hidalgo, United Kingdom) housed in a comfortable chest-worn harness, and analysed using LabChart Pro 7

(ADInstruments, Australia). ECG traces were visually inspected with artefacts removed from analysis. HRV was derived for 5-minute ECG epochs with <5% artefact. Fast Fourier transformation was performed to determine the high frequency (HF) spectral component (0.15-0.40Hz), providing a validated reflection of parasympathetic activity [11] presented in normalised units (HFnu %; i.e., as a proprtion of total power in the 0.04-0.4Hz range). Tri-axial accelerometery provided an index of bodily orientation (upright, supine, prone) and movement speed (stationary, moving slowly, or moving fast). These data, in conjunction with autonomic parameters and self-reported sleep times were used to designate sleep / wake periods, and to identify periods of daytime lying down. Heart rate (HR) and HRV was processed for the entire 24-hour period both before and after the challenge, with specific time segments identified for when the participant was asleep (at night) and awake (the total 24-hour period with the time spent asleep subtracted).

2.3. Statistical analyses

Analyses were performed using Stata 14, with two-tailed significance set at $p<0.05$. Potential differences in demographic and clinical characteristics between challenge groups were explored using independent samples *t*-tests and Pearson χ^2 tests. Mixed repeated-measures analysis of variance was used to examine the trajectory of fatigue over time in response to challenges. Pearson correlations were conducted to explore pairwise associations between key variables. Linear mixed models (LMM; with random intercepts by participant and robust standard errors) were used to explore behavioural (sleep duration and quality, proportion of daytime hours spent lying down) and autonomic (HR and HRV, controlling for age) changes in response to challenges. The interaction between challenge time and wakefulness was also explored for HR and HRV to examine if the shift in autonomic balance during the transition from wakefulness to sleep was affected by the challenge.

3. Results

Demographic and clinical characteristics of the participant sample are reported in Table 1; these did not significantly differ across challenges (all $p>0.10$). All participants were non-smokers. As previously reported [2] both PHYS and COG challenges induced an exacerbation of the fatigue state. A main effect ($F(2,66)=12.63$, $p<0.001$, $\eta_p^2=0.28$) and quadratic trend ($F(1,33)=6.80$, $p=0.014$, $\eta_p^2=0.17$) of time was observed; fatigue increased from baseline immediately after completing the challenges, and remained elevated 24-hours after challenges (Table 1). No significant main effect of challenge, nor challenge × time interaction was identified. Given this, and the similarity in demographic and clinical characteristics, the data were collapsed across challenges for subsequent analyses.

Table 1. Descriptive and clinical characteristics at baseline, and fatigue in response to challenge, of participants with chronic fatigue syndrome (CFS) who completed physical (n = 24) or cognitive (n = 11) challenges.

	Physical (PHYS) challenge		**Cognitive (COG) challenge**	
	M	SD	M	SD
Age (years)	36.0	10.3	36.7	9.4
Sex				
Female (n; %)	15	62.5%	4	36.4%
Male (n; %)	9	37.5%	7	63.6%
Body mass index (kg/m^2)	22.5	3.2	23.8	2.7
Moderate to vigorous physical activity (hours / week)	1.4	1.1	1.9	2.2
Physical symptoms (SOMA^; 0-12)	5.8	3.1	5.7	3.4
Retrospective sleep quality (PSQI*; 0-21)	7.0	3.8	7.5	3.8
Fatigue (FES global score, 0-10)				
Baseline	4.4	1.6	4.8	1.2
0h post-challenge	5.6	2.3	6.9	1.7
24h post-challenge	5.8	2.3	6.4	2.0

^ SOMA scores ≥ 3 indicate clinically significant fatigue; * PSQI scores ≥ 5 indicate poor sleep quality.

Sleep, activity, and autonomic parameters during the post-exertional exacerbation of fatigue are shown in Figure 1. LMM analyses identified that sleep quality and duration was comparable pre- and post-challenge; however the proportion of daytime hours spent lying down was significantly greater post-challenge (B=4.17±1.85, p=0.024, 95%CI:0.54,7.81). As expected, a significant decrease in HR (B=-17.76±1.00, p<0.001, 95%CI:-19.72,-15.79) and increase in HRV (B=12.87±1.49, p<0.001, 95%CI:9.95,15.79) between wake and sleep was found. No significant effect of challenge time (pre-challenge vs. post-challenge) was found for HR or HRV; however a significant challenge time × wakefulness interaction was identified for HRV, with the shift in HRV between wakefulness and sleep decreasing post-challenge (B=-2.91±1.20, p=0.016, 95%CI: =-5.26,-0.55). The inclusion of daytime inactivity (i.e., the proportion of daytime hours spent lying down) in the regression models of autonomic activity elicited no change in the parameter estimates. Pairwise correlations demonstrated a significant association between poorer sleep quality (from PSQI) and reduced pre-challenge nocturnal HRV (r(34)=-0.41, p=0.014); however no significant associations between autonomic parameters and changes in sleep and activity measures were found.

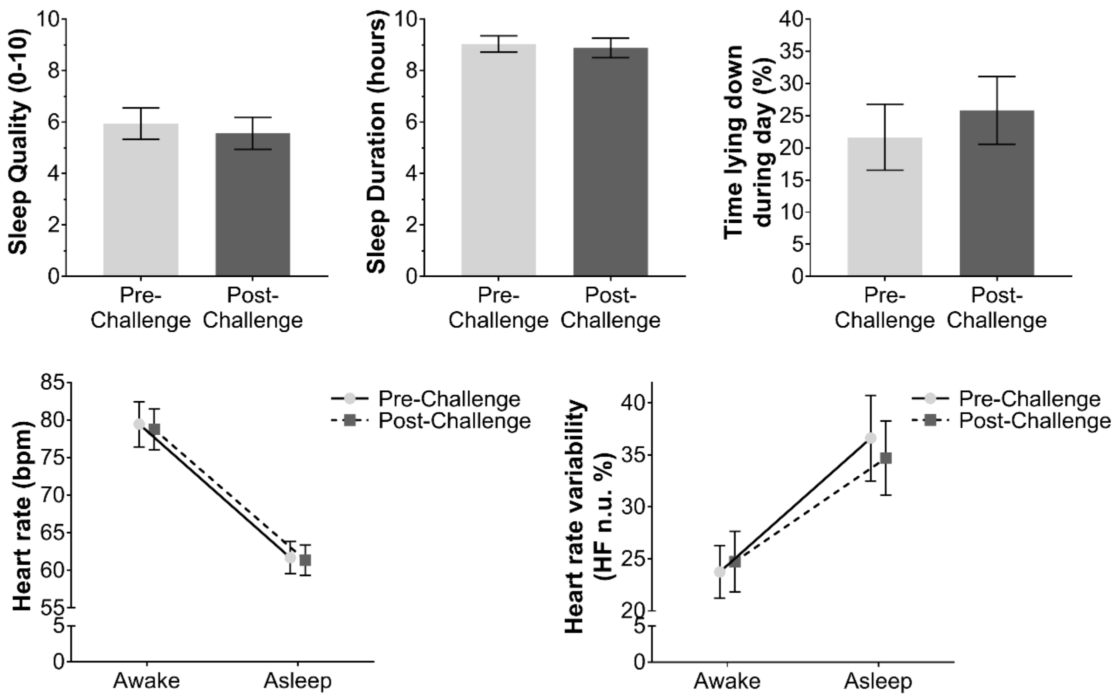

Figure 1. Sleep, physical activity, and autonomic activity of participants with chronic fatigue syndrome (n=35) before (pre-challenge) and after (post-challenge) completing physical or cognitive challenge. Data are presented as means, with error bars indicating 95% confidence intervals.

4. Discussion and Conclusion

This preliminary study examined autonomic and behavioural parameters in participants with CFS before and after they completed fatiguing cognitive or physical challenges. Both challenges induced an exacerbation of self-reported fatigue, which remained elevated 24-hours post-challenge. As hypothesised, participants spent a greater proportion of daytime hours lying down after completing a challenge, yet contrary to our hypothesis reported comparable duration and quality of sleep duration pre- and post-challenge. HR and HRV showed the expected, normal diurnal modulations with the sleep / wake cycle [22, 23], yet the magnitude of increase in HRV between wake and sleep was significantly reduced after completing the challenge, suggestive of reductions in nocturnal parasympathetic activity during post-exertional worsening of symptoms in CFS.

Diurnal changes in parasympathetic, vagal activity reflected by HRV serve an important role in the 'falling asleep' process. Gradual increases in vagal activity are typically observed during the transition from wakefulness to sleep, peaking in the early hours of the sleep cycle during restorative, slow wave (deep) sleep [23-25]. Our correlational analyses were commensurate with previous studies demonstrating a link between greater nocturnal HRV and better sleep quality in healthy and clinical populations [26-28]. However, we did not observe a significant reduction in self-reported sleep quality accompanying reduced nocturnal HRV during the post-challenge period; this might reflect a lack of sensitivity in subjective sleep quality measures, as well as a loss of specificity when using HRV averaged across the night (i.e., collapsed across different sleep stages, which inherently differ in HRV [23]). The use of polysomnography in future studies would allow a more detailed examination of the impact of physical and cognitive challenges on HRV during specific sleep stages, and their influence on the experience of post-exertional fatigue.

Notable limitations of the study are that participants were recruited from a specialist tertiary-care clinic, and although experiencing significant impairment, they may have been more functional than others who are unable to undertake outpatient treatment or tolerate challenge protocols. It is possible that individuals with more severe fatigue and functional disability would have greater symptom exacerbation in response to challenges, accompanied by more prominent alterations in autonomic and behavioural parameters. The amalgamating of cognitive and physical challenges, although eliciting comparable fatigue exacerbation, also limits the conclusions that can be drawn. Further investigation with larger-sized samples and consideration of additional covariates (e.g., mood symptoms) is required before the mechanisms responsible for the observed alterations in HRV can be established, and the clinical implications of these findings determined.

Conflict of Interest Statement

The authors declare that they have no competing interests.

Acknowledgements

This work was supported by research grants from the Mason Foundation (CT23137; CT29128). AL is supported by a Fellowship from the National Health and Medical Research Council of Australia (No. 510246). The supporting agencies had no role in study design, data collection, analysis and interpretation, manuscript preparation or submission. The generous involvement of the participants is gratefully acknowledged.

Conflicts of interest
Dr Cvejic: nothing to disclose
Dr Sandler: nothing to disclose
Dr. Keech: nothing to disclose
Dr. Barry: nothing to disclose
Prof. Lloyd: nothing to disclose
Prof. Vollmer-Conna: nothing to disclose

References

[1] Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A, The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group, Ann Intern Med 121 (1994) 953-959. doi: 10.7326/0003-4819-121-12-199412150-00009.

[2] Keech A, Sandler CX, Vollmer-Conna U, Cvejic E, Lloyd AR, Barry BK, Capturing the post-exertional exacerbation of fatigue following physical and cognitive challenge in patients with chronic fatigue syndrome, J Psychosom Res 79 (2015) 537-549. doi: 10.1016/j.jpsychores.2015.08.008.

[3] Cook DB, Light AR, Broderick G, Sheilds MR, Dougherty RJ, Meyer JD, VanRiper S, Stegner AJ, Ellingson LD, Neural consequences of post-exertion malaise in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Brain Behav Immun 62 (2017) 87-99. doi: 10.1016/j.bbi.2017.02.009.

[4] Sandler CX, Lloyd AR, Barry BK, Fatigue Exacerbation by Interval or Continuous Exercise in Chronic Fatigue Syndrome, Med Sci Sports Exerc 48 (2016) 1875-1885. doi: 10.1249/MSS.0000000000000983.

[5] Van Cauwenbergh D, Nijs J, Kos D, Van Weijnen L, Struyf F, Meeus M, Malfunctioning of the autonomic nervous system in patients with chronic fatigue syndrome: a systematic literature review, Eur J Clin Invest 44 (2014) 516-526. doi: 10.1111/eci.12256.

[6] Meeus M, Goubert D, De Backer F, Struyf F, Hermans L, Coppieters I, De Wandele I, Da Silva H, Calders P, Heart rate variability in patients with fibromyalgia and patients with chronic fatigue syndrome: a systematic review, Semin Arthritis Rheum 43 (2013) 279-287. doi: 10.1016/j.semarthrit.2013.03.004.

[7] Staud R, Autonomic dysfunction in fibromyalgia syndrome: postural orthostatic tachycardia, Curr Rheumatol Rep 10 (2008) 463-466. doi: 10.1007/s11926-008-0076-8.

[8] Kadota Y, Cooper G, Burton AR, Lemon J, Schall U, Lloyd A, Vollmer-Conna U, Autonomic hyper-vigilance in post-infective fatigue syndrome, Biol Psychol 85 (2010) 97-103. doi: 10.1016/j.biopsycho.2010.05.009.

[9] Fagundes CP, Murray DM, Hwang BS, Gouin JP, Thayer JF, Sollers JJ, 3rd, Shapiro CL, Malarkey WB, Kiecolt-Glaser JK, Sympathetic and parasympathetic activity in cancer-related fatigue: more evidence for a physiological substrate in cancer

survivors, Psychoneuroendocrinology 36 (2011) 1137-1147. doi: 10.1016/j.psyneuen.2011.02.005.

[10] Tak LM, Riese H, de Bock GH, Manoharan A, Kok IC, Rosmalen JG, As good as it gets? A meta-analysis and systematic review of methodological quality of heart rate variability studies in functional somatic disorders, Biol Psychol 82 (2009) 101-110. doi: 10.1016/j.biopsycho.2009.05.002.

[11] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, Heart rate variability: standards of measurement, physiological interpretation and clinical use, Circulation 93 (1996) 1043-1065. doi: 10.1161/01.CIR.93.5.1043.

[12] Mizuno K, Tanaka M, Yamaguti K, Kajimoto O, Kuratsune H, Watanabe Y, Mental fatigue caused by prolonged cognitive load associated with sympathetic hyperactivity, Behav Brain Funct 7 (2011) 17. doi: 10.1186/1744-9081-7-17.

[13] Segerstrom SC, Nes LS, Heart rate variability reflects self-regulatory strength, effort, and fatigue, Psychol Sci 18 (2007) 275-281. doi: 10.1111/j.1467-9280.2007.01888.x.

[14] Hautala A, Tulppo MP, Makikallio TH, Laukkanen R, Nissila S, Huikuri HV, Changes in cardiac autonomic regulation after prolonged maximal exercise, Clin Physiol 21 (2001) 238-245. doi: 10.1046/j.1365-2281.2001.00309.x.

[15] Calandra-Buonaura G, Provini F, Guaraldi P, Plazzi G, Cortelli P, Cardiovascular autonomic dysfunctions and sleep disorders, Sleep Med Rev 26 (2016) 43-56. doi: 10.1016/j.smrv.2015.05.005.

[16] Burton AR, Rahman K, Kadota Y, Lloyd A, Vollmer-Conna U, Reduced heart rate variability predicts poor sleep quality in a case-control study of chronic fatigue syndrome, Exp Brain Res 204 (2010) 71-78. doi: 10.1007/s00221-010-2296-1.

[17] Boneva RS, Decker MJ, Maloney EM, Lin JM, Jones JF, Helgason HG, Heim CM, Rye DB, Reeves WC, Higher heart rate and reduced heart rate variability persist during sleep in chronic fatigue syndrome: a population-based study, Auton Neurosci 137 (2007) 94-101. doi: 10.1016/j.autneu.2007.08.002.

[18] Sandler CX, Hamilton BA, Horsfield SL, Bennett BK, Vollmer-Conna U, Tzarimas C, Lloyd AR, Outcomes and predictors of response from an optimised, multidisciplinary intervention for chronic fatigue states, Internal Med J 46 (2016) 1421-1429. doi: 10.1111/imj.13251.

[19] Hadzi-Pavlovic D, Hickie IB, Wilson AJ, Davenport TA, Lloyd AR, Wakefield D, Screening for prolonged fatigue syndromes: validation of the SOFA scale, Soc Psychiatry Psychiatr Epidemiol 35 (2000) 471-479. doi: 10.1007/s001270050266.

[20] Hickie IB, Davenport TA, Hadzi-Pavlovic D, Koschera A, Naismith SL, Scott EM, Wilhelm KA, Development of a simple screening tool for common mental disorders in general practice, Med J Aust 175 Suppl (2001) S10-17.

[21] Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ, The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research, Psychiatry Res 28 (1989) 193-213. doi: 10.1016/0165-1781(89)90047-4.

[22] Elsenbruch S, Harnish MJ, Orr WC, Heart rate variability during waking and sleep in healthy males and females, Sleep 22 (1999) 1067-1071. doi: 10.1093/sleep/22.8.1067.

[23] Baharav A, Kotagal S, Gibbons V, Rubin BK, Pratt G, Karin J, Akselrod S, Fluctuations in autonomic nervous activity during sleep displayed by power spectrum analysis of heart rate variability, Neurology 45 (1995) 1183-1187. doi: 10.1212/wnl.45.6.1183.

[24] Chouchou F, Desseilles M, Heart rate variability: a tool to explore the sleeping brain?, Front Neurosci 8 (2014) 402. doi: 10.3389/fnins.2014.00402.

[25] Tobaldini E, Nobili L, Strada S, Casali KR, Braghiroli A, Montano N, Heart rate variability in normal and pathological sleep, Front Physiol 4 (2013) 294. doi: 10.3389/fphys.2013.00294.

[26] Irwin MR, Valladares EM, Motivala S, Thayer JF, Ehlers CL, Association between nocturnal vagal tone and sleep depth, sleep quality, and fatigue in alcohol dependence, Psychosom Med 68 (2006) 159-166. doi: 10.1097/01.psy.0000195743.60952.00.

[27] Werner GG, Ford BQ, Mauss IB, Schabus M, Blechert J, Wilhelm FH, High cardiac vagal control is related to better subjective and objective sleep quality, Biol Psychol 106 (2015) 79-85. doi: 10.1016/j.biopsycho.2015.02.004.

[28] Yang AC, Tsai SJ, Yang CH, Kuo CH, Chen TJ, Hong CJ, Reduced physiologic complexity is associated with poor sleep in patients with major depression and primary insomnia, J Affect Disord 131 (2011) 179-185. doi: 10.1016/j.jad.2010.11.030.

Highlights

- Substantive and prolonged exacerbation of fatigue was triggered by physical or cognitive challenges
- A greater proportion of daytime hours were spent lying down post-challenge
- Sleep duration and quality were comparable pre- and post-challenge
- Nocturnal parasympathetic activity was reduced post-challenge