ALLOSTATIC OVERLOAD AND ITS MITIGATING FACTORS IN THE WHIRLWIND OF THE COVID-19 ERA

PhD thesis

Dóra Blanka Békési, MD

Károly Rácz Doctoral School of Clinical Medicine

Semmelweis University

Supervisor: Ajándék Eőry, MD, Ph.D

Official reviewers: Zsófia Drobni, MD, Ph.D
Dalma Kellermayer, MD, Ph.D

Head of the Complex Examination Committee:
Zoltán Rihmer, MD, Ph.D D.Sc

Members of the Complex Examination Committee:
Xénia Gonda, MA, Ph.D, PharmD
László Kolozsvári, MD, Ph.D

Budapest
2023

Introduction

The concept of stress and its role in health and disease stimulates continuously expanding research. Individual vulnerability towards stress is determined by genetic, behavioural, and environmental factors, all interacting constantly throughout life to shape one's risk to and resilience against diseases. The brain is an essential coordinator when it comes to individual reaction to stress, and it discriminates threatening stimuli from benign ones. When the brain and the body are able to keep the physiological systems of the body fluctuating to meet demands from external forces, a balanced state called allostasis is maintained. The threshold of stimuli that tips out this balance differs in individuals. But it is universal that subtle and long-lasting life situations as well as threatening challenges which change the individual's living conditions, social and family circles, and work may all be sources of cumulative load. If stress does not resolve, the body remains on high alert, and eventually it learns how to cope with higher stress levels by continuous secretion of stress hormones, thus arrives in the state of allostatic load. Repeated load on the body, the elevated activity and changes of the physiological systems and the wear and tear on tissues and organs develop pathologies, thus, they cumulate and lead to disease. The clinical definition of allostatic overload (AO) identifies a state where accumulation of life events exceeds individual resources and may endanger one's health.

With COVID-19 we were facing an excessive stressor that superimposed on other life events. It proved to be a trigger that can

push individuals into the state of allostatic overload. The pandemic especially put a tremendous burden on health care professionals, who were now facing a professional challenge on top of a personal one. In an era of a pandemic, the ultimate goal is to be able to prevent overwhelming stress or to decrease the negative impact of it on health by finding effective and conscious tools against it, like physical activity or recreational activities.

Objectives

We intended to measure allostatic overload from a clinimetric perspective, specifically focusing on the first wave of COVID-19. We investigated among two specific groups for research purposes.

We explored allostatic overload and well-being in an aging general population sample, who practiced regular, uniform, moderately intensive aerobic exercise (3-1-2 meridian exercise).

We evaluated the prevalence of allostatic overload among Hungarian general practitioners as well and defined its most important predictors. We measured their well-being, forms, and regularity of recreational activity they practiced to increase mental and physical health, as well as resilience against stress load.

We were to verify the following hypotheses:

I. The infection itself and the health care confinements both might have contributed to the stress burden of an aging population, but we postulated that among those, who practice regular 3-1-2 meridian exercise with the aim of active health preservation, the

prevalence of AO would be lower than in those who practice it irregularly or do not at all.

II. Our further hypothesis was that due to the active health-preserving activity – those who regularly practiced 3-1-2 meridian exercise, had better physical well-being than those who did not.

III. Working in the frontline, GPs were exposed to the infection while having had to provide adequate care to their patients in adverse circumstances. We assumed that these aspects accumulated in high prevalence of AO.

IV. Among GPs we aimed to assess individual habit of recreation and postulated that regular recreation was associated with lower prevalence of AO.

Methods

Sample and Measures

We conducted two cross-sectional research after the first wave of the COVID-19 pandemic. We performed a voluntary and anonymous online survey on platform Google Forms between 21 May and 1 September 2020 among certified 3-1-2 meridian exercise instructors and their communities and we collected data among Hungarian general practitioners (GPs) between 28 August and 16 October 2020. All participants were recruited via email, using the official mailing list of certified 3-1-2 meridian instructors and institutional sources of Hungarian GPs. In our invitation letter we clarified that the Family

Medicine Department at Semmelweis University was the conductor of the survey and claimed the necessary time frame to complete it (15-20 minutes). We did not offer monetary or non-monetary incentives. Personal data was not collected in either case and accordingly we performed data analysis anonymously, but we generated an ID code for each participant in both data collection for a possible follow up. Online consent was given by all participants. Both surveys were constructed in a way that all answers had to be given to the items of the measurement tools to continue with the survey; therefore, we did not need to exclude anyone due to incomplete reply to any questions. Inclusion criteria were above 18 years of age and understanding of Hungarian language. Participants needed to be willing to complete the survey. Exclusion criteria were under 18 years of age, no access of the online platform, and insufficient understanding of Hungarian language. Both studies were conducted by the Declaration of Helsinki and was approved by the review board of the Medical Research Council (IV/5657-2/2020/EKU).

We collected basic *sociodemographic data*: like age, gender, place of living, working conditions, number of acute diseases, number of chronic diseases, self-reported psychiatric conditions, drug consuming habits, and need of health care services during restrictions.

We measured *COVID-related allostatic overload* based on the Diagnostic Criteria for Psychosomatic Research Semi-Structured Interview (DCPR-SSI). It measures allostatic overload via items related to stress factors (A1 criterion), the perceived burden of these

factors (A2 criterion) with stressor-related distress symptoms (B1 criterion), social (B2 criterion) or environmental inadequacies (B3 criterion). We used the Psychosocial Index (PSI), which is a self-rating questionnaire to cover each criterion.

We measured *distress symptoms* with the short version of Depression, Anxiety and Stress Scale (DASS-21), and Kellner Symptom Questionnaire (SQ), while we used the Public Health Surveillance Well-being Scale (PHS-WB) besides SQ to measure *well-being*.

In our non-clinical sample, we mapped the frequency of practicing *3-1-2 meridian exercise*, as well as how long it has been practiced. It is a Chinese 30-minute uniformed medium-intensity aerobic physical exercise performed identically by thousands in all areas of Hungary coordinated by hundreds of certified instructors. It is known and practiced worldwide with the purpose of health preservation, has no contraindications, and can be easily performed by the older generations as well. Its characteristics meet the WHO recommendations of physical activity. We grouped our participants based on the frequency of meridian exercise practice to match WHO recommendation, to those who practiced exercise frequently as recommended (at least 30 minutes 3-5 times weekly) (fPE), those who practiced regularly but the frequency did not reach the recommendation (1-2 times weekly) (PE) and those who did not practice at all or practice irregularly. Latter meant our control group.

In our Hungarian GP sample, we mapped *recreational activities*, which are rewarding experiences that are personally meaningful and

help the individual arrive in the present, disengage from the burdens and boost resilience. We offered multiple recreational categories for our participants, but also, they were able to provide their own individual answers on their sources of recreation as well. They were asked about the number of days when they chose to take time to do recreational activities for at least 30 minutes during a week. We grouped them based on the number of days they take at least 30 minutes for recreation: 5-7 days, 3-4 days, and 0-2 days were determined for frequency. Latter meant our control group.

Statistical Analysis

We used a mixed method. Qualitative analysis was applied to assess the most burdening challenges during the pandemic and recreational activities of GPs. Following qualitative analytical guidelines all free text responses were systematically read by all members of our research group, blocks of text that reported factors contributing to allostatic overload were identified, and provisional code names were assigned to them. We then compared our codes and agreed on common ones, which were then re-examined. We then identified themes to organise coded answers into higher-level concepts that explained the origins of overload, while constantly checking their interpretation with the original data, and agreeing on a final list of categories.

In our quantitative analysis we used Chi square tests in case of categorical data, two-tailed t-test for normally-, and Kruskal-Wallis test for non-normally distributed continuous variables. Post hoc we

applied Dunn's pairwise tests with Bonferroni adjustment for multiple comparisons of the three pairs of groups. Normality of data was assessed by Kolmogorov-Smirnov test. In both cases step forward likelihood ratio logistic regression was applied to identify predictors of AO. In the case of our non-clinical sample general linear model was applied to measure the effect of the regularity of physical exercise on SQ total well-being adjusting for sex, age, and chronic diseases, while in the case of GPs, step forward likelihood ratio logistic regression was also used to measure the effect of the number of days when at least 30-minute recreation was practiced by the respondents on allostatic overload. We applied 95% confidence intervals (CI). In all cases a p value < 0.05 was considered statistically significant. We applied SPSS-24.0 software (SPSS Inc., Armonk, NY, USA).

Results

Sociodemographic Data, Physical Exercise and Recreation

Altogether 442 non-clinical adults and 228 GPs completed the surveys. Proportion of women was 92% in our non-clinical sample and 68% in our GP sample.

In our non-clinical sample, 62% of adults were retired, 20% went to their workplace and 12% worked in home office (6% did not provide information on their work circumstances). The sample was not representative due to gender disproportion. According to sex we did

not find any statistically significant differences in health-related and sociodemographic characteristics.
49% practiced exercise frequently, at least 3-5 times a week (fPE) while 27% did less regularly, 1-2 times a week, not reaching the recommended 3-5 times a week frequency (PE) and 24% did not practice or did irregularly (controls).

97% of GPs worked actively throughout the first wave of the pandemic. 68% worked in person. All of them used mixed – personal, phone calls/video calls and online – consultation forms. This sample was not representative either due to gender disproportion. According to sex we did not find any statistically significant differences in health-related and sociodemographic characteristics in this sample either.
All together large percent of GPs turned out to do actively for their health. 95% GPs reported they do recreational activities with the purpose of conscious health prevention. 43% of them even spare 30 minutes for recreation at least on 5 days a week. 33% do 30-minute recreation 3-4 days a week and 24% do in only 0-2 days a week. The median number of different marked recreation types was 4 (IQR: 3,5).

Allostatic Overload

Allostatic overload with physical symptoms of distress, impaired social and occupational functioning or declined psychological well-being was experienced by 29% (n=128) of the normative sample, although 33.5% (n=148) of the non-clinical sample reported that COVID-related changes exceeded their coping abilities. Those who

did 3-1-2 meridian exercise regularly (fPE) were statistically significant less likely to develop allostatic overload comparing to controls ($\chi 2(1) = 5.6$; $p=0.018$). After adjusting for age, sex, and the number of chronic diseases, each individual life stressor (PSI items of A1 criterion) increased the likelihood of allostatic overload by 20% (OR:1.19, CI [1.06 -1.36], p=0.005) and anxiety symptoms measured by the Kellner's Symptom Questionnaire by 18% (OR: 1.18, CI [1.13-1.24], p<0.001).

Allostatic overload with physical symptoms of distress, impaired social and occupational functioning or declined psychological well-being was experienced by 57% of the GPs, although 60% of the GPs reported that COVID-related changes exceeded their coping abilities. Female sex (OR: 1.99, CI [1.06 - 3.74], p<0.032) increasing number of individual life stressors (PSI items of A1 criterion) (OR: 1.4, CI [1.2 - 1.6], p<0.001) increased the likelihood of allostatic overload. Additionally, we found that each more day, when time was spared for recreation, lowered the odds of AO by 20% (OR: 0.838, CI [0.72 - 0.97], p=0.020) after adjusting for age, place of living and chronic diseases.

Distress Symptoms, Well-being

Doing 3-1-2 meridian exercise at least 3-5 times a week (fPE) was found to be associated with decreased symptoms of anxiety, and depression as well. While somatization symptoms proved to be non-significant between exercise groups and controls, the final somatization scale showed better results in the fPE group due to higher

scoring on Kellner's QS subscale of physical well-being. Total well-being reached higher scores in the exercising groups and the same good results were shown on both mental and physical aspects of it. After adjusting for age, sex and chronic diseases, a significant effect of exercise on well-being outlined ($F(2, 435)=225.0$, $p<0.001$). Planned contrasts revealed that both fPE ($p<0.001$, 95% CI [1.4-3.9]) and PE ($p=0.043$, 95% CI [0.04 -2.83]) associated with significantly higher well-being, compared to control group.

We also found that being involved in 30 minutes of recreation at least 5 days a week was associated with lower scores on symptoms of anxiety, depression, somatisation, and hostility, while 30-minute recreation on 3-4 days weekly was associated with elevated mental and physical well-being scores.

Qualitative results

According to our qualitative data analysis, the most disturbing issue people faced during the lock-down was the obligatory quarantine resulting in lack of personal contacts and loneliness. This challenge appeared among GPs' answers as well, but most of them reported professional issues like work-related conditions and increased workload as most challenging. Interestingly both groups suffered from unavailability of specialist care. GPs were unable to refer their patients to necessary specialist care, thus, lack of professional help due to the burden of COVID-19 that afflicted specialized health institutions tormented both populations we examined. Besides decreased availability for outpatient specialty care, undeveloped proceeding

rules and structural changes in delivering care stood as most bothering circumstances for our GPs. Among personal challenges both samples reported wearing a mask and sanitizing, increased home workload, organization, online education, curfew, travelling restrictions, opening restrictions, misleading information, uncertainty, financial problems, loss of loved ones and loss of mental balance as challenging.

While in our non-clinical sample, the health-prevention activity was given by 3-1-2 meridian exercise, we investigated recreational activities among GPs. The most popular categories turned out to be connection with nature, reading, watching movies and physical exercise.

Conclusions

The pandemic not only impacted the general population but burdened medical professionals cumulatively. Examining a non-clinical regularly exercising aging population we were able to monitor the positive influence of moderate intensity aerobic exercise on mental and physical well-being as well as its potential protecting effect against allostatic overload. Investigating Hungarian general practitioners, we could find correlations between their recreational habits and their well-being as well as reduced levels of depressive and anxiety symptoms, somatization, and hostility. Our main findings regarding our hypotheses can be summarized as follow:

I. We found that among the non-clinical participants the lack of personal contact, the confinements, and the panic and fear due to uncertainty were the most challenging aspects of the pandemic. 29% of the participants met the criteria of allostatic overload.

II. Those who practiced 3-1-2 meridian exercise regularly (at least 3-5 times a week) with the aim of health preservation presented statistically significant less depressive and anxiety symptoms, than those who did not. They also maintained better mental and physical health as compared to the control group and were statistically significant less likely to develop allostatic overload. Somatization symptoms differed statistically not significant between exercise groups and controls, however, the final somatization scale showed better results in the fPE group due to the increased physical well-being.

III. The pandemic and the related confinements of proceeding rules resulted in significantly increased stress load of health care professionals. General practitioners – as frontline workers – faced doubled challenges, personal and professional, and the latter was not only related to the increasing number of infections and consequent life-threatening conditions, but – through the disrupted communication and facilities – to the care for their chronically ill patients. Additionally, they suffered from communication pressure and psychological burden of their own and patient-related fears. Facing all these challenges simultaneously, 57% of the Hungarian general practitioners

experienced allostatic overload during the first wave of the COVID-19 pandemic in our study.

IV. Ninety five percent of the general practitioners reported to do actively for their health by spending at least 30 mins on recreation on average 4 days a week. 30 minutes of recreation 3-4 days a week was associated with increased mental, and physical well-being, while 30 mins of recreation 5-7 days a week was associated with reduced levels of depressive and anxiety symptoms, somatization, and hostility besides increased well-being.

Bibliography of the candidate's publications

Békési Dóra, Teker Illés, Torzsa Péter, Kalabay László, Rózsa Sándor, Eőry Ajándék. To prevent being stressed-out: Allostatic overload and resilience of general practitioners in the era of COVID-19. A cross-sectional observational study. Eur J Gen Pract. 2021;27:277–85.

Eöry Ajándék, Békési Dóra, Eöry Ajándor, Rózsa Sándor. Physical Exercise as a Resilience Factor to Mitigate COVID-Related Allostatic Overload. Psychother Psychosom. 2021;90:200–6.