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Vital Signs and Sensors for Post-Exertional Malaise Prevention

Abstract: Post-exertional malaise (PEM) is the core symptom of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis, a disease that can break out after surviving a SARS-CoV-2 infection. Multiple types of triggers lead to an extremal deterioration of the patient's overall health condition. In this paper, vital signs are compared to what extent they are sensitive to the triggers and thus can be used to prevent PEM. In addition, sensors and measurement methods are proposed, based on criteria for use in patients' daily lives. Even simple pedometers can contribute to PEM prevention. However, chest straps and wrist-worn sensors are more promising. The essential relevant vital parameters heart rate, blood pressure and respiratory rate are measured in this way.

Keywords: ME/CFS, Post-Covid, Longhaul Covid, post exertional neuro immune exhaustion, pacing

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1 Introduction

Covid-19 infection leads to post viral symptoms such as fatigue, muscle pain, post-exertional malaise (PEM) and brain fog in a proportion of those infected [1]. These symptoms can already occur in mild courses and younger patients. If these symptoms occur over a longer period, they are referred to as post Covid syndrome, long Covid, chronic Covid or the long-haul Covid.

The exact cause is as unclear as the number of people affected. It is estimated that the prevalence of suffering from long-term effects after a Covid-19 is 30 % [2], which is below the prevalence rates of the SARS pandemic at the beginning of the century of about 40 % with ongoing chronic fatigue [3]. An initial preprint suggests that in 50 % of the patients the

diagnosis of chronic Covid-19 is congruent with the diagnosis of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (ME/CFS) [4]. ME/CFS is a severe neuroimmunological disease. Symptoms of the disease include non-restorative sleep, a substantial decrease or impairment in activity level, PEM, cognitive impairment, and orthostatic intolerance [5].

The use of questionnaires is a proven approach to access PEM. Therefore, the DePaul Post-Exertional Malaise Questionnaire was established [6]. In contrast, PEM can be measured by the objective 2-day cardiopulmonary exercise test. This test shows changes in energy production and physiological function. Thus, functional impairment and significantly reduced exercise capacity are detected on the second day [7]. In everyday life, PEM will mainly be induced by four triggers. These include: physical stress, cognitive stress, emotional stress and orthostatic stress. As shown in Figure 1, PEM is distinguished by a delayed onset and general symptom exacerbation lasting from hours to weeks [8,9].

Previous publications have targeted monitoring of Covid-19 symptoms [10]. However, in chronic Covid-19 and ME/CFS, PEM is the core symptom that provides a drastic loss of quality of life. Prevention of PEM can prevent overall symptom worsening and should therefore be pursued as a high priority. It should be noted that monitoring itself can be a burden for patients. Therefore, the aim of this paper is to discuss appropriate vital signs and sensors for PEM monitoring. In particular, the various triggers of PEM are discussed and a recommendation is made regarding a general coverage of PEM triggers in order to effectively use the applied energy for monitoring and not be limited by the sensors themselves. The overall goal is to strengthen PEM prevention and improving patient's quality of life.

In this paper, we will discuss the following: (i) vital signs and their suitability for PEM prevention based on the responsiveness to the four PEM triggers mentioned above and (ii) derived sensors for the everyday life of patients with corresponding conditions. The main recommendations are summarized and an outlook on future development is given.

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Figure 1: Post-exertional malaise is characterized by delayed onset, symptom worsening and variable duration triggered by different events.

2 Vital Signs for PEM Prevention

In this section, vital signs are discussed in terms of their suitability for PEM prevention. For this purpose, the four traditional vital signs are: heart rate (HR), body temperature (BT), blood pressure (BP) and respiratory rate (RR). In addition, physical activity (PA) is considered. PA refers to moderate or vigorous aerobic (endurance) physical activity, which is recommended to be at least 30 minutes 5 days per week [11].

Other vital signs such as pain (counts as a direct symptom of ME/CFS), blood glucose levels (no continuous, non-invasive measurement), and oxygen saturation (no expected response to most PEM triggers) are not considered further.

2.1 Method for Comparison

The vital parameters are evaluated on the basis of a numerical scale. It is evaluated whether the corresponding vital parameter reacts to the corresponding PEM triggers. There are three gradations: 0=low, 1=moderate, 2=high. High denotes a strong change in the biosignal with directly measurable changes. If more complex signal processing algorithms are required to make the changes visible, the sensitivity is labeled as moderate. If there is no change in the vital parameter or if it can only be made visible using highly complex or offline signal processing algorithms, the sensitivity of the signal is rated low.

The evaluation regarding the number of publications is performed in two levels: 0=few publications (less than five), 1=mentioned in many publications (equal or more than five). Using the search term ("post exertional malaise" OR "post exertional neuroimmune exhaustion") AND ("me" OR "cfs" OR "seid" OR "cfids" or "me/cfs"), eligible studies were located in a database search on Scopus. Scopus was used to get

a quantitative overview of reviewed articles. Inclusion criteria included the use of objective, noninvasive criteria to measure PEM in ME/CFS. Of 227 articles screened, 26 were finally included.

2.2 Results and Discussion

Table 1 shows the parameters to be compared with the evaluation in terms of trigger sensitivity and number of publications. This results in an overall summed score. Although a subjective estimate was given, the ranking determined is also reflected in previous guides for patients recommending heart rate measurements [12]. Nevertheless, the exact score should only be seen as a general orientation and indication of the suitability of the corresponding vital sign for PEM monitoring.

Heart rate. HR as a cardiovascular vital sign has the highest score here and thus offers itself as the best vital sign for monitoring PEM. This is mainly due to a good sensitivity to the different PEM triggers. Heart rate responds to physical triggers and increases under stress. Emotional impact is also strongly reflected in heart rate. Due to the impaired response of the orthostatic system in people with ME/CFS, heart rate also increases significantly when standing. A response to cognitive load is also measurable, but weaker.

Blood Pressure. BP is equally suitable for general monitoring of PEM triggers. BP responds strongly to physical activity as well. Orthostatic stress in connection with the accompanying symptomatology "orthostatic hypotension" leads to a strong drop in blood pressure after standing up. In response to emotional stress, blood pressure increases strongly. For cognitive stress, on the other hand, the blood pressure response is weaker.

Respiratory Rate. RR is a vital sign that responds rapidly to changes; RR increases in response to both physical and orthostatic triggers. Similarly, the effects of cognitive and emotional triggers can be measured in respiratory rate. However, the changes are less pronounced than in BP or HR.

Physical Activity. PA as a vital sign, according to our definition, includes physical activity as a trigger of PEM. By extension, when moderate and intense exertion are further classified, the proportion of standing, lying, and sitting also falls into PA and thus the information about orthostatic triggers. Hereby, PA as a vital sign is unrelated to emotional or cognitive triggers in its immediate response. This is not to be confused with PA decreasing as a consequence of these triggers by PEM.

Body Temperature. The slight changes in BT due to cognitive influences are difficult to detect due to general artifact susceptibility to heat, sweating and clothing. The same

applies to changes due to a change in body position. Emotional triggers, on the other hand, lead to stronger temperature changes and physical triggers in this context to the strongest change in body temperature. Due to the low sensitivity to most PEM triggers and strong susceptibility to interferences, BT will not be considered further in the following.

Table 1: Comparing vital signs regarding their sensitivity to PEM triggers. Comparison regarding the following triggers: physical P, cognitive C, emotional E, orthostatic O.

Vital Sign	Trigger Sensitivity				Publications	Summed Score*
	P	C	E	O		
HR	High	Moderate	High	High	Many	8
BT	High	Low	Moderate	Low	Few	3
BP	High	Moderate	High	High	Many	8
RR	High	Moderate	Moderate	High	Many	7
PA	High	Low	Low	High	Many	5

* Points: high = 2 ; moderate = 1 ; low = 0 ; many = 1 ; few = 0

3 Derived Sensors for PEM Prevention

After discussing vital signs in terms of their suitability for PEM prevention, this section evaluates sensors and measurement principles considering real world requirements. Electrocardiography (ECG), photoplethysmography (PPG), actigraphy (AG), and spirometry (SM) are compared as common, non-invasive methods of measuring vital signs in everyday life.

3.1 Analysis regarding Daily-Life Requirement

There are patient-side requirements for methods of measuring vital signs. On the one hand, the handling of the sensor should be as simple as possible, on the other hand, the measurement method should allow a high signal quality. The following criteria are introduced for this purpose: Comfort when worn, suitability for long-term measurements, attachment, accuracy of the sensor and coupling of interference sources.

Comfort is classified as high if freedom of movement is not impaired, for example when wearing the sensor on the wrist or hip. Medium comfort refers to minor restrictions on movement, for example due to a chest strap, and low comfort severely restricts natural movement. In the case of long-term measurement, a distinction is made between whether the

measurement can be performed continuously or not. A measurement duration of more than 15 minutes is evaluated taking the battery time into account. The time frame corresponds to a planned activity in which there is a risk of triggering PEM. The attachment is classified as easy, if no wiring is required due to the measurement method and little consideration has to be given to the sensor placement. Moderate attachment requires special sensor placement and heavy sensor attachment cannot be done independently. Accuracy is quantitatively described as the signal-to-noise ratio and susceptibility to artifacts in the signal. Furthermore, the biosignals to be detected are mentioned. The comparisons are based on our own considerations.

3.2 Results and Discussion

PPG. PPG is a useful measurement method for determining the vital signs suitable for PEM monitoring. Blood volume fluctuations under the skin are measured via light and thus HR is determined over time. The RR can also be determined via amplitude and/or frequency modulation. In addition, blood pressure can also be determined from the combination of several PPG sensors by calculating the pulse wave transit time. The PPG is characterized by a high degree of user-friendliness, as the sensors can be placed directly on the skin and do not require any special placement. The application is therefore often found on wrists, for example in smartwatches. In use, the color of the skin can affect the signal quality of the PPG.

ECG. In contrast, an ECG is characterized by better signal quality, combined with higher demands on the sensors, the attachment and placement. Measurement of electrical heart activity is the gold standard in clinical practice for HR measurement. In modern devices, a measurement can be performed via chest straps. Measurements via a smartwatch are also possible, but only when a finger is placed on the device and therefore not continuously. Due to the high signal quality, the ECG is also suitable for precisely temporally resolving the individual contractions of the heart muscles and thus also for analyzing heart rate variability (HRV).

AG. Possibilities for AG measurements via triaxial accelerometers are nowadays already feasible with mobile devices. Pedometers can be easily attached to the body at the hip and measure the activity via the number of steps. Attaching an accelerometer to the chest allows measurement of chest movement and thus respiration rate, but is vulnerable to other body movements.

SM. A spirometer measures temporal changes in the volume of air inhaled and exhaled and can thus very accurately determine respiratory volumes and RR. This requires breathing through the device, which is very uncomfortable for

patients and is therefore not performed over a long period of time.

The assessment for applicability in everyday life can still differ for the measurement methods, depending on the specific sensor used. A general overview is given in this section without any claim to completeness. The results are summarized in Table 2. Other methods such as electrooculography, electroencephalography and electromyography were not considered further due to their very high susceptibility to interference in everyday life. Cuff-based blood pressure measurements were not considered here due to two limitations: (i) the very precise sensor positioning requirements, which otherwise leads to greater inaccuracy (ii) the high variability of readings, which complicates PEM monitoring.

Table 2: Comparison regarding daily-life requirements and biosignals to be measured. Quantitative comparison criteria are applied, see section 3.1.

Meas. Method	Wearer Comfort	LT-Monitoring	Attachment	Accuracy	Vital Signs
ECG	Medium	Yes	Medium	High	HR,RR
PPG	High	Yes	Easy	Medium	HR,RR,(BP)
AG	High	Yes	Easy	Medium	PA,(RR)
SM	Low	No	Easy	High	RR

4 Conclusion & Outlook

In this paper, vital signs were discussed in terms of their suitability for PEM prevention. Heart rate, blood pressure, and respiratory rate are the most sensitive to the PEM triggers studied. Monitoring physical activity and respiratory rate can provide additional support, whereas monitoring body temperature is not suitable to avoid PEM. Without further medical background knowledge, patients should monitor pure changes in their parameters as a first step. In the future, intelligent processing algorithms can support evaluation and analysis.

The evaluation of sensors and measurement principles in this paper reveal that modern PPG sensors are ideally suited to monitor a wide range of vital signs. PPG sensors can be effortlessly integrated into modern smartwatches, for example. Heart rate and respiration rate can be determined from the blood volume pulse, and blood pressure can also be measured with the help of another PPG sensor. ECG accuracy comes with a more complex sensor attachment. Chest straps are a compromise. However, the better signal quality allows analysis of other parameters such as heart rate variability. In general, heart rate and respiratory rate can be recorded via ECG and PPG.

Predicting post-exertional malaise in ME/CFS or chronic Covid-19 is difficult due to the lack of defined criteria, heterogeneity in the patient population, the wide variation in symptoms and triggers along with the overall poor understanding of the disease. A large inter- and intra-patient variance complicates specific rule making for vital sign monitoring in PEM avoidance strategies. In the future, technical support will make it possible to process more information and better interpret the complex interrelationships between different measurement parameters, thus supporting patients in their daily lives.

Author Statement

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