

Electroencephalogram and electrocardiograph activity association to state of fatigue in university students

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Abstract

Fatigue is a commonly reported issue in the young adult population with severe consequences on one's physical and mental well-being if left untreated. This study aimed to investigate the relationship between fatigue levels, heart rate variability (HRV), and electroencephalogram (EEG) frequency waves during eyes open resting state, as well as general correlation between ECG and EEG activity. Previous studies have shown that effects of fatigue can be found in both ECG and EEG recordings. However, the participants were performing tasks when being observed. This study aimed to replicate their findings during simple resting state. Moreover, it looked at potential correlations between the ECG and EEG activity. 40 participants (aged between 18 and 30) included in this study all completed the Multidimensional Fatigue Inventory (MFI) questionnaire, and the collected data was divided into two groups: fatigued and not fatigued students. Four separate correlation analyses were conducted, involving HRV, mean heart rate, alpha1, alpha2, theta and fatigue status under eyes open conditions. A negligibly small significant effect was found on certain components of HRV positively correlating to alpha1 and theta waves. And only RMSSD turned out to have a negative significant effect on fatigue state. No significant outcomes were found in correlation between the examined EEG activity and fatigue. This lack of significant results suggests that in past research the task conditions might have worked as a better condition for measuring fatigue. Furthermore, it highlights the need for further research into the relationship between ECG and EEG activity.

Keywords: Fatigue, ECG, EEG, alpha1, alpha2, theta, HRV

Introduction

About half of both the older and the younger adult population experiences general fatigue (Yoshikawa et al., 2014). Fatigue is a difficulty in initiating or preserving attention and voluntary actions (Güneş & Demirer, 2022). Characterized by a reluctance to try, an impairment of efficiency, consciousness, and overall mental functioning, fatigue is defined as a subjective state that extends beyond mere tiredness and affects the execution of tasks and obligations, while it cannot be predicted based on the amount of effort exerted (Strahler et al., 2016). A distinction between physical fatigue and mental fatigue is made (Mohammadi et al., 2021). Physical fatigue is a bodily weakness that can occur because of repetitive muscle activity (Tanaka et al., 2012) and is obtained and increased by higher levels of physical exercise (Mohammadi et al., 2021). In contrast, mental fatigue is a psychobiological state in which a decrease in cognitive performance resulting from long-term periods of cognitive activity can be detected (Mohammadi et al., 2021).

In general fatigue, disturbed sleep is the biggest predictor, with high immersion in work, high work demands, low social support, and being a female acting as contributing factors (Åkerstedt et al., 2004). More specifically, individuals who are affected by psychological factors such as depression, emotional stress, or anxiety are more prone to feeling fatigued compared to those who do not have these psychological issues (Chen, 1986). Moreover, physical inactivity is also identified as a risk factor (Chen, 1986).

Furthermore, it has been found that about 10% of young and middle-aged adults experience levels of fatigue so severe that it interferes with their personal lives, with damaging effects on function and ability to work, cognitive ability, and emotional well-being (Strahler et al., 2016). The influence of stress, particularly chronic stress, appears to play a major role in the development and persistence of fatigue (Strahler et al., 2016). Therefore, it is not surprising that it negatively affects the quality of life of especially university students by causing a decline in academic performance, a decrease in attention, higher stress levels, and poorer physical health (Güneş & Demirer, 2022). All this makes fatigue of significant concern in university students as it holds a considerable impact on daily activities of young adults (Yoshikawa et al., 2014).

Historically, mental fatigue has mostly been studied with the electroencephalogram (EEG), strongly suggesting that mental fatigue can result in obvious changes in EEG signals (Li et al., 2020).

The EEG data is made of waveforms most often categorised by frequency. Consequently,

EEG waves are named after their frequency range using Greek numerals. The most commonly studied waveforms include delta that is seen in deep sleep (0.5 to 4Hz); theta which is brought on by drowsiness (4 to 7Hz); alpha which is observed during mental relaxation (8 to 12Hz), and beta which is the most frequently seen rhythm in a normally functioning brain during the day (13 to 30Hz) (Nayak & Anilkumar, 2019).

When measuring fatigue, the EEG bands are often divided into narrower bands. The distinction between lower alpha or alpha1 (8-10 Hz) and higher alpha or alpha2 (10-13 Hz) bands is made to reduce the risk of frequency effects being either cancelled out or not discovered, while also making the statistical results more significant (Li et al., 2020). Previous studies have shown that while alpha2 desynchronization is positively correlated with memory and cognitive behaviour, alpha1 rhythm is associated with attention, and its power increases with the increase of fatigue level, making the alpha1 band better for fatigue detection (Li et al., 2020).

When it comes to research on fatigue, specifically alpha and theta frequencies in the awake EEG are of particular interest. Alpha waves indicate the state of relaxation and wakefulness (Li et al., 2020), meaning that during active wakefulness (with eyes open), alpha power is usually low (Strijkstra et al., 2003). With mental fatigue increasing, the power of alpha rhythm increases as well (Li et al., 2020).

When entering a state of sleep from resting conditions with eyes closed a steady increase in theta power has been observed (Strijkstra et al., 2003). Theta waves are thus considered to reflect the early state of sleepiness, which is related to brain fatigue. Reduced alpha power and increased theta power during resting awake periods might therefore indicate a high motivation for sleeping (Strijkstra et al., 2003).

Although an electrocardiogram (ECG) is considered to be one of the most important sources for fatigue indicators (Hu & Lodewijks, 2020), little information can be found on ECG in resting state of healthy participants. In fact, Huang et al. (2018) proved that a mental fatigue state can be detected with a reasonable CV accuracy (up to 75.5%) by a convenient wearable ECG device. The CV accuracy is a ratio of the correctly predicted observations to the total observations (Huang et al., 2018). Overall, heart rate (HR) and heart rate variability (HRV) have been linked to fatigue and workload. HRV refers to the beat-to-beat variation in intervals in heartbeat within ECG and is made out of different parameters such as SDNN, RMSSD, VLF, HF, LF, and HF (Ellenbroek et al., 2019). Studies done with drivers and specifically pilots have shown that HR relates to different levels of task difficulty during a simulated flight, while HRV is susceptible to the mental workload (Hu & Lodewijks, 2020).

Contrary to low frequency (LF) of HRV which correspond to lower wakefulness characteristics, high frequency (HF) of HRV indicate sleepy characteristics (Hu & Lodewijks, 2020). All this makes ECG a good way to measure fatigue, however, more research on non-stimulated healthy subjects is needed.

The simultaneous use of ECG and EEG to detect fatigue has been proven to be more effective than the use of EEG alone (Laurent et al., 2013; Zhao et al., 2012). While plenty of data can be found that supports the strong coupling between the cardiac and EEG activities during sleep, less is known about the state of sleep deprivation and fatigue.

A study by Kokonozi et al. (2008) looked at the EEG and ECG recordings of sleep-deprived subjects exposed to real driving conditions. They tried to discover to what extent the brain and heart lose complexity in a synchronous way, and with that, a possible interaction between the two systems. The results of the four observed subjects showed the existence of low to intermediate cross-correlation between the pairs of biological oscillators. Later on, Hamdi et al. (2019) found a Granger causality within and between ECG and EEG signals. Granger causality is used for revealing whether a one time series is useful for predicting another. It does not imply a direct cause-and-effect relationship but rather indicates predictive causality based on the idea that a variable X can predict another variable Y, meaning that the past values of X should be able to give additional information when predicting the future values of Y that go beyond what could be predicted using only the past values of Y itself (Roebroek, 2015).

This study aims to fill in the gap on the already existing research on fatigue and its effects on ECG activity. Furthermore, it seeks to examine the correlation between heart rate variability and the different EEG frequency waves in eyes open resting state. The study expects to find a positive correlation between HRV and alpha1, alpha2, and theta frequency waves. As well as higher values for all examined variables individually (HRV, alpha1, alpha2, and theta waves) in fatigued individuals.

Methods

Participants

There were 74 of participants, varying in ages between 17 and 53 taking part in this research. 58 of the participants were female. At the time of the study, most of the subjects were first year psychology students of the bachelor program at Tilburg University. They were compensated for their participation in participation credits. No specific inclusion or exclusion criteria were defined. Out of the 74 tested participants, 71 were included in data analysis based on the age criteria. As the study focused on fatigued university student population, the age range between 18 and 30 was chosen. The participants were presented with an information letter and had to give written consent in order to participate in the study. This research was approved by the ethical committee of Tilburg School of Social and Behavioural Sciences.

Questionnaire

To study the fatigue levels of the included participants, the Multidimensional Fatigue Inventory (MFI) scale (Shahid et al., 2011) was used. The MFI is a 20-item scale designed to evaluate five dimensions of fatigue: reduced motivation, reduced activity, general fatigue, physical fatigue, and mental fatigue. It is a self-report, pencil-and-paper measure requiring between 5 to 10 min for completion. The questionnaire asks participants to rate their recent well-being, using a 7-point Likert's scale. Statements include phrases like 'physically I can take on a lot', 'I can concentrate well', and 'I tire very easily'. Positively phrased items are reverse-scored, and an overall higher total score corresponds with more acute levels of fatigue (Shahid et al., 2011).

This standardised questionnaire has often been used in fatigue studies. Namely, Lou et al. (2001) used it to measure the physical and mental fatigue in Parkinson's disease and found that PD patients scored higher than the healthy controls in all of the five dimensions of fatigue. The scale has been tested and validated for its psychometric properties in a variety of participant populations, including cancer patients receiving radiotherapy, patients with the chronic fatigue syndrome, medical students and junior physicians, and psychology students (mean age of 24 years) (Smets et al., 1995).

Developers of the MFI scale reported an internal consistency ranging from .53 to .93. and test-retest variability of 0.7 to 0.87 (Shahid et al., 2011). Moreover, results of Smets et al. (1995) by and large, support the validity of the MFI.

Procedure

The experiment was run on the OpenSesame program (Mathod, Schreij, & Theeuwes, 2012). Three various simple cognitive tasks were performed before the resting state was recorded. The instructions were written in white font, size 100 on a black computer screen, and the participants were asked to press the space button when they were ready to begin the experiment. Now they simply had to relax and sit still for five minutes, concentrating on the white cross presented to them in the middle of the black display, until the writing on the screen would tell them that the experiment is finished. For the eyes closed condition, the same was asked of them, but since this time the participants eyes would be closed, the test leader would let them know when the experiment ended, and they could open their eyes again. Both of the conditions were performed in complete silence.

Before starting the data collection, participants were informed about the experiment and gave their written consent. Next, they were fitted with an EEG cap and electrooculogram (EOG) flat sensors were placed on their face to measure eye movement and account for the blink correction. Furthermore, two ECG flat sensors were placed on their chest. Once the preparation was done, they were led to a sound-reducing cabin equipped with an EEG amplifier and stimulation computer on which the experiment would be run. The cabin was also supplied with a CCTV camera that made it possible for the participants to be observed during the experiment from the outside, and a microphone/speaker to enable communication between the subject and the test leader. The participant was sat about 60cm away from the monitor with a resolution of 1920px x 1080px on which the experiment was run. Prior to starting the experiment, the lights were dimmed, and the participants asked to stay as still as they could, in order to limit the amount of noise picked up by the EEG recording system. Since the experiment for this research is based on the resting condition, the participants were simply asked to sit in front of the screen and focus on the plus displayed there for five minutes. Following this they again sat back and relaxed for five minutes, but this time with their eyes closed.

Because this research was done in collaboration with other experiments, the participants have already completed three cognitive tasks prior to the start of the resting state measurements. After finishing the entire set of experiments, the participants filled out several questionnaires, including the standardised Multidimensional Fatigue Inventory scale that was used in this study.

Physiological measurements

The EEG recording of a 5-minute resting-state EEG and ECG with eyes open and eyes closed were recorded with a BioSemi Active-Two amplifier system (BioSemi, Amsterdam, The Netherlands). The 32 Ag/AgCl of the EEG electrodes were positioned on the elastic cap according to the 10/20 system and digitized at a sampling rate of 512 Hz, with a reference electrode (Common Mode Sense: CMS) fixed between Cz and C3 (online reference). Offline reference electrodes were placed on both the left and right mastoid, while the ground electrode was located between Cz and C4.

Furthermore, four EOG and two ECG flat electrodes were used in this research. Two of the EOG sensors were positioned above and underneath the eye, measuring vertical eye movement, and two on the outer canthi of both the left and the right eye, measuring horizontal EOG.

The two ECG electrodes were positioned in the middle of the sternum and on the left rib cage at 10 cm below the armpit, roughly corresponding to the standard positioning of the V1 versus V6 lead. This configuration has been demonstrated to produce an ECG signal where the R-peak was prominent in comparison to the other ECG phenomena, which aids in the determination of the R-peaks. The data was sampled at a rate of 512 Hz.

Pre-processing

The EEG data analysis was performed using the program BrainVision Analyzer (Version 2.2.2, Brain Products GmbH, Gilching, Germany) and re-referenced offline using the average of left and right mastoids. Next, the data was filtered offline with a low cutoff of .01 Hz, a high cutoff of 30 Hz, and a 50 Hz notch filter.

The data was split into two intervals, eyes open and eyes closed. To analyse the frequency content of the EEG signals, the Fast Fourier Transform (FFT) analysis was performed. The FFT is a widely used mathematical technique that reveals the underlying frequency components present in the data. Allowing for the identification and characterization of major frequency bands in the EEG signals. To make the data less noisy, the Welch spectrum method was implemented. This means that the long EEG signal was cut into smaller segments, with some overlap between successive segments. The short spectra were then averaged to obtain a smoothed and more reliable estimate of the power spectral density.

Data was also corrected for eye movements using a procedure of Gratton & Coles

(Gratton et al., 1983).

The R-peak scoring of the ECG data was done using the algorithm described by Afonso et al. (1999). While the HRV data was calculated using the RHRV package (RHRV_4.2.7; Rodriguez-Linares et al. 2022) in the R statistical program (R Core Team 2023). The data was first bandpass filtered 1- 256 Hz, but the Afonso et al. (1999) algorithm used filter banks that limited the effective signal bandwidth to 5.6 - 28 Hz. The interbeat intervals were eliminated if their deviation from the mean exceeded 3 standard deviations from the mean. These removed intervals were reinserted back into the series using a cubic splines function. The LF/HF ratio was also calculated.

Statistical analysis

The statistical analyses were done in SPSS (IBM SPSS Statistics for Windows, version 28.0.1.0, 2021). The statistical analyses focused on the comparing the ECG and EEG activity of fatigued and non-fatigued individuals in the eyes open condition. The frequency ranges chosen for the examined alpha and theta waves comply to those commonly found in literature. So, alpha was divided to alpha1 with a frequency of 8 – 10 Hz, and alpha2 with a frequency of 10 – 12 Hz and were collected over the posterior scalp. More specifically, the topographical maximum for alpha1 and alpha2 was found at the occipital lobe, with alpha1 waves spreading to the parietal lobe, making these areas appropriate for analysis. Theta rhythms were gathered over the mid-line frontal positions, within the frequency domain of 4- 8 Hz.

Levels of fatigue are included in this study as the independent discrete quantitative variable. The dependent variables in this experiment are eyes open state, heart rate variability and the activity in the posterior and midline frontal areas of the brain. These are continuous quantitative variables.

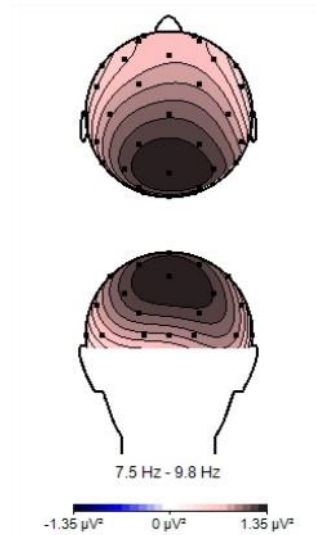
Visual inspection of the EEG and ECG data did not indicate outliers.

To study the hypotheses that there is a correlation between HRV and EEG activity, and people with increased levels of fatigue people have a higher HRV and higher alpha activity in the eyes open condition and reduced alpha power and increased theta power in the eyes closed condition, multiple correlation analyses were performed in SPSS.

Each correlation analysis included the status of fatigue, eyes open, HRV activity, and a specific combination of electrodes, based on the frequency examined. Based on the heatmap produced in Brain Vision Analyzer (Version 2.2.2, Brain Products GmbH, Gilching, Germany) the following electrodes were chosen to represent the specific brainwave

frequencies. The alpha1 data included the electrodes Pz, CP1, CP2, P3, P4, PO3, PO4, Oz, O1, O2. The alpha 2 data consisted of the following electrodes PO3, PO4, Oz, O1, O2. The theta data was made out of the electrodes Fz, Cz, FC1, FC2.

Figure 1: heatmap of alpha1 (7.5 to 10 Hz)



This study mainly focused on the interaction between HRV and EEG frequency activity with respect to the level of fatigue. Before running the actual analyses, the assumptions of correlations were checked for each separate analysis. The assumptions of independence of observations and normality were met.

Results

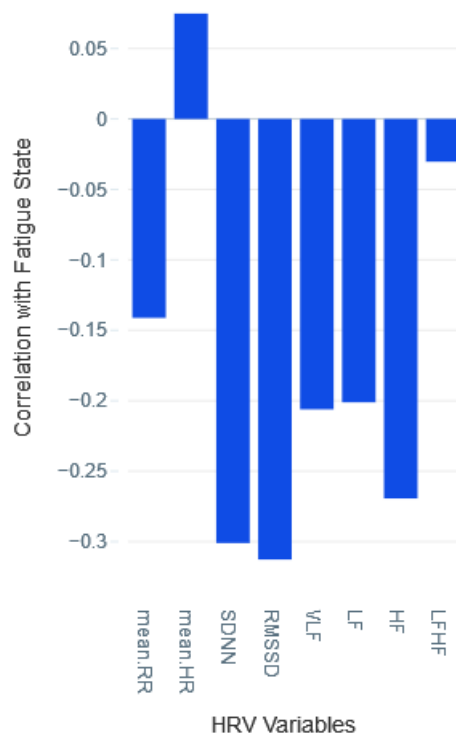
The outcomes of the questionnaire showed that none of the participants scored severely high or low on their levels of fatigue. The overall score of the MFI included the following levels of fatigue: 2 (not fatigued, N=21), 3 (neither fatigued nor not fatigued, N= 32), 4 (fatigued, N= 18). Subsequently, the data was split into two groups of fatigued and not fatigued for further analysis.

As mentioned in the methods section, four separate correlation analyses were performed. All of them included HRV, mean HR and fatigue status and operated under the eyes open condition. One analysis simply explored the relationship between HRV, mean HR and fatigue status. The second analysis also regarded the alpha1 waves, as the correlation was expected to be the highest there. The third included alpha2 waves. And lastly theta waves were analysed.

Correlation fatigue with HRV and mean HR

The fatigue state is only positively correlated with mean HR (-0.748) and negatively correlated with all of the HRV components, indicating that higher fatigue levels are associated with lower heart rate variability (HRV) measures. There is a moderate correlation with SDNN (-0.301) and RMSSD (-0.313) and a weak negative correlation with LF (-0.201) and HF (-0.269). However, RMSSD is the only component with statistical significance ($p = 0.049$). None of the other correlations between either mean HR or HRV components and fatigue are statistically significant ($p > 0.05$).

Figure 2: graph of HRV values and mean HR in correlation with fatigue status



Correlation alpha1 with fatigue HRV, mean HR and during eyes open

There are no strong or statistically significant correlations between alpha1 waves and fatigue state. Most correlations between HRV and alpha1 waves are weak and non-significant, with absolute values ranging from 0.008 to 0.479. The parietal lobe (electrodes Pz, P3, P4, CP1, CP2) show a positive moderate to strong (0.502 to 0.369) statistically significant ($p < 0.05$) correlation with the LF/HF (0.369 to 0.502) component of heart rate variability.

Correlation fatigue with HRV, mean HR and alpha2 during eyes open

There is a weak negative correlation between alpha2 waves and fatigue state, however it is not statistically significant. The values of mean R-R, SDNN, RMSSD VLF, LF, and HF carry a positive correlation to alpha2 waves. The mean HR and LF/HF have a weak correlation with alpha2 waves. However, all of the observed correlations are weak and non-significant ($p > 0.05$), with absolute values ranging from 0.012 to 0.237.

Correlation fatigue with HRV, mean HR and theta during eyes open

There is a weak negative correlation between theta waves and fatigue state, however it is not statistically significant. The theta band power at the examined EEG electrodes shows weak to moderate positive correlations with all HRV metrics and the mean HR. The absolute values range from 0.013 to 0.500. However, only the two of the values are statistically significant: SDNN ($p < 0.05$) and VLF ($p < 0.01$).

Discussion

This study examined the correlation between heart rate variability and fatigue state, as well as the correlation of different EEG frequency waves and fatigue state in eyes open resting state. Furthermore, the correlation between HRV and EEG frequency waves was examined. The study expected to find a correlation of HRV with alpha1, alpha2, and theta frequency waves. And a higher HRV as well as increased alpha1, alpha2, and theta power in more fatigued individuals.

The results showed no significant effect of fatigue on all HRV components, except for RMSSD which showed a moderate negative effect. A negative correlation shows that reduced HRV values are associated with higher levels of fatigue, which is the opposite of the made prediction. RMSSD assesses the variability in the time intervals between consecutive heartbeats. It provides information about the short-term variability of heart rate and reflects the activity of the parasympathetic nervous system, which is responsible for promoting relaxation and recovery (Malik et al., 1996). This correlation suggests that fatigue may influence the parasympathetic nervous system's regulation of heart rate variability.

Furthermore, there were no significant effects of fatigue on the EEG frequency bands. There was little statistically significant correlation between the HRV components and EEG frequencies. The positive significant correlation of alpha1 waves of the parietal lobe with the LF/HF component of heart rate variability indicates a possible connection between autonomic

nervous system activity and cortical brain activity. The LF/HF ratio used as an indicator of sympathetic-vagal balance. It suggests that the balance between sympathetic and parasympathetic activity, as reflected in the LF/HF ratio, may influence the modulation of alpha1 oscillations in the brain (Malik et al., 1996). Further analysis is needed to determine the specific nature and direction of the correlation.

Another statistically significant finding of this study indicates a positive correlation between SDNN, VLF power, and theta waves. This suggests that as the amplitude or power of theta waves increases, SDNN and VLF power in HRV also increase. SDNN is a measure of overall HRV that represents the standard deviation of all the normal-to-normal (NN) intervals between consecutive heartbeats. It reflects the total variability in heart rate and is influenced by both parasympathetic and sympathetic nervous system activity (Malik et al., 1996). VLF power represents the spectral power in the very low-frequency range (usually below 0.04 Hz). VLF power is associated with various physiological processes, including thermoregulation, hormonal fluctuations, and renin-angiotensin system activity (Malik et al., 1996). The correlation implies a possible relationship between specific autonomic nervous system activity and the modulation of theta brainwave activity. Additional analysis is required to establish the precise characteristics and orientation of the correlation.

The lack of significant results in the performed research could be ascribed to a number of different reasons. Firstly, most of the already existing research that has found significant results controlled for the levels of experienced immediate fatigue. For example, Kokonozi et al. (2008) had their participants stay awake for 24 hours, resulting in approximately equal amounts of fatigue. This leads to a very precise insight in the effect of the immediate state of fatigue. In this study, the experienced fatigue was determined by a MFI questionnaire, indicating a general state of fatigue, which could account for the lessened effect of fatigue on examined variables.

Moreover, previous studies such as Kokonozi et al. (2008) had their participants perform tasks, sometimes in combination of resting state, rather than only observing the resting state. A difference in task performance could be a better fatigue indicator, as it forces the participants to react. This could show higher differences between fatigue states compared to a simple resting state.

Additionally, the lack of the fatigue status working as an indicator for both HRV and EEG in this study could be ascribed to the fact that none of the participants scored extremely low(1) or high(5) on the MFI questionnaire. Meaning that the research presented worked with levels of fatigue that were moderate at best. This could account for the lack of effect of

fatigue on all of the variables and the correlation between them. Furthermore, the detected fatigue in the sample population was surprisingly low, with only 19 participants scoring a 4 on levels of fatigue. The comparison was made between moderately not fatigued participants (21) and moderately fatigued persons (18), making the sample very small. This could account for fatigue playing such a low indicator role.

In short, this study looked at how status of fatigue might correlate to ECG activity or EEG activity, and how the ECG activity correlates to specific EEG frequencies independent of fatigue. It has found no significant effect of fatigue status on EEG frequencies (alpha1, alpha2, theta). Therefore, unable to prove the hypothesis that higher fatigue is associated with increased EEG waveform power. A significant negative correlation between RMSSD of heart rate variability and fatigue status was found, disproving the hypothesis of higher levels of HRV predictors being associated with higher fatigue. There was also no significant effect on correlation between alpha2 waves and any of the HRV variables. While a significant positive correlation was found between alpha1 waves and the LF/HF component of HRV, and between theta waves and SDNN and VLF values, which somewhat confirms the hypothesis of a positive correlation between HRV and alpha1 and theta frequency waves. However, when comparing these results to the significant results found in studies that control levels of fatigue, it shows a clear discrepancy. Moreover, studies that include a task condition have found a more significant effect, compared to resting state. The lack of overlap in findings expresses the need for more research on levels of fatigue and its correlation with HRV. More research is also needed in correlation of HRV with cortical brain frequencies.

References:

- Åkerstedt, T., Knutsson, A., Westerholm, P., Theorell, T., Alfredsson, L., & Kecklund, G. (2004). Mental fatigue, work and sleep. *Journal of Psychosomatic Research*, 57(5), 427–433. <https://doi.org/10.1016/j.jpsychores.2003.12.001>
- Afonso, V., Tompkins, W., Nguyen, T. Q., & Luo, S. (1999). ECG beat detection using filter banks. *IEEE Transactions on Biomedical Engineering*, 46(2), 192–202. <https://doi.org/10.1109/10.740882>
- BrainVision Analyzer (Version 2.2.2) [Software]. (2021). Gilching, Germany: Brain Products GmbH.
- Ellenbroek, B. A., Kidwell, M., Colussi-Mas, J., & Youn, J. (2019). *Heart Rate Variability as a Translational Biomarker for Emotional and Cognitive Deficits*. <https://doi.org/10.1016/b978-0-12-803161-2.00013-8>
- Gratton, G. Coles, M.G.H., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, 55, 468-484.
- Güneş, M., & Demirer, B. (2022). A Comparison of Caffeine Intake and Physical Activity According to Fatigue Severity in University Students. *Evaluation & the Health Professions*, 46(1), 92–99. <https://doi.org/10.1177/01632787221141504>
- Hamdi, S., Bedoui, M. H., & Chaabane, N. (2019). *Intra and Inter Relationships between Biomedical Signals: a VAR Model Analysis: Vol. IV*. 2019 23rd International Conference Information Visualisation. <https://doi.org/10.1109/IV.2019.00076>
- Hu, X., & Lodewijks, G. (2020). Detecting fatigue in car drivers and aircraft pilots by using non-invasive measures: The value of differentiation of sleepiness and mental fatigue. *Journal of Safety Research*, 72, 173–187. <https://doi.org/10.1016/j.jsr.2019.12.015>
- Huang, S., Li, J., Zhang, P., & Zhang, W. (2018). Detection of mental fatigue state with wearable ECG devices. *International Journal of Medical Informatics*, 119, 39–46. <https://doi.org/10.1016/j.ijmedinf.2018.08.010>
- IBM Corp. (2021). IBM SPSS Statistics for Windows, Version 28.0.1.0. Armonk, New York: IBM Corp.

- Kokonozzi, A., Michail, E., Chouvarda, I., & Maglaveras, N. (2008). A study of heart rate and brain system complexity and their interaction in sleep-deprived subjects. *Computing in Cardiology Conference*. <https://doi.org/10.1109/cic.2008.4749205>
- Laurent, F., Valderrama, M., Besserve, M., Guillard, M., Lachaux, J., Martinerie, J., & Florence, G. (2013). Multimodal information improves the rapid detection of mental fatigue. *Biomedical Signal Processing and Control*, 8(4), 400–408. <https://doi.org/10.1016/j.bspc.2013.01.007>
- Li, G., Xiao, Q., Xu, W., Jiao, W., Jiang, Y., Gao, Z., & Zhang, J. (2020). The impact of mental fatigue on brain activity: a comparative study both in resting state and task state using EEG. *BMC Neuroscience*, 21(1). <https://doi.org/10.1186/s12868-020-00569-1>
- Lou, J., Kearns, G. L., Oken, B., Sexton, G., & Nutt, J. G. (2001). Exacerbated physical fatigue and mental fatigue in Park-inson's disease. *Movement Disorders*, 16(2), 190–196. <https://doi.org/10.1002/mds.1042>
- Malik, M., Bigger, J. T., Camm, A. J., Kleiger, R. E., Malliani, A., Moss, A. J., & Schwartz, P. J. (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, 17(3), 354–381. <https://doi.org/10.1093/oxfordjournals.eurheartj.a014868>
- Method, S., Schreij, D., & Theeuwes, J. (2012). OpenSesame
- Mohammadi, A., Nematpour, L., & Dehaghi, B. F. (2021). Reader fatigue – Electroencephalography findings: A case study in students. *Work-a Journal of Prevention Assessment & Rehabilitation*, 1–6. <https://doi.org/10.3233/wor-205121>
- Nayak, C. S., & Anilkumar, A. C. (2019, March 24). *EEG Normal Waveforms*. Nih.gov; StatPearls Publishing. Retrieved June 19, 2023, <https://www.ncbi.nlm.nih.gov/books/NBK539805/>
- R Core Team (2023). A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>
- Rodriguez-Linares L, Vila X, Lado M, Mendez A, Otero A, Garcia C (2022). RHRV_4.2.7
- Roebroeck, A. (2015). Granger Causality. *Brain Mapping*, 593–597. <https://doi.org/10.1016/b978-0-12-397025-1.00337-7>
- Shahid, A., Wilkinson, K., Marcu, S., & Shapiro, C. M. (2011). Multidimensional Fatigue Inventory (MFI). *Springer EBooks*, 241–243. https://doi.org/10.1007/978-1-4419-9893-4_57

- Smets, E. M. A., Garssen, B., Bonke, B., & De Haes, J. (1995). The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*, *39*(3), 315–325. [https://doi.org/10.1016/0022-3999\(94\)00125-o](https://doi.org/10.1016/0022-3999(94)00125-o)
- Strahler, J., Doerr, J. M., Ditzen, B., Linnemann, A., Skoluda, N., & Nater, U. M. (2016). Physical activity buffers fatigue only under low chronic stress. *Stress*, *19*(5), 535–541. <https://doi.org/10.1080/10253890.2016.1192121>
- Strijkstra, A. M., Beersma, D. G. M., Drayer, B., Halbesma, N., & Daan, S. (2003). Subjective sleepiness correlates negatively with global alpha (8–12 Hz) and positively with central frontal theta (4–8 Hz) frequencies in the human resting awake electroencephalogram. *Neuroscience Letters*, *340*(1), 17–20. [https://doi.org/10.1016/s0304-3940\(03\)00033-8](https://doi.org/10.1016/s0304-3940(03)00033-8)
- Tanaka, M., Shigihara, Y., Ishii, A., Funakura, M., Kanai, E., & Watanabe, Y. (2012). Effect of mental fatigue on the central nervous system: an electroencephalography study. *Behavioral and Brain Functions*, *8*(1), 48. <https://doi.org/10.1186/1744-9081-8-48>
- Yoshikawa, T., Tanaka, M., Ishii, A., & Watanabe, Y. (2014). Association of Fatigue with Emotional-Eating Behavior and the Response to Mental Stress in Food Intake in a Young Adult Population. *Behavioral Medicine*, *40*(4), 149–153. <https://doi.org/10.1080/08964289.2013.833082>
- Zhao, C., Zhao, M., Liu, J., & Zheng, C. (2012). Electroencephalogram and electrocardiograph assessment of mental fatigue in a driving simulator. *Accident Analysis & Prevention*, *45*, 83–90. <https://doi.org/10.1016/j.aap.2011.11.019>

Appendix



MFI® MULTIDIMENSIONAL FATIGUE INVENTORY

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Instructions:

By means of the following statements we would like to get an idea of how you have been feeling **lately**. There is, for example, the statement:

"I FEEL RELAXED"

If you think that this is **entirely true**, that indeed you have been feeling relaxed lately, please, place an **X** in the extreme left box; like this:

yes, that is true 1 2 3 4 5 **no, that is not true**

The more you **disagree** with the statement, the more you can place an **X** in the direction of "no, that is not true". Please do not miss out a statement and place only one **X** in a box for each statement.

1	I feel fit.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
2	Physically, I feel only able to do a little.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
3	I feel very active.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
4	I feel like doing all sorts of nice things.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
5	I feel tired.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
6	I think I do a lot in a day.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
7	When I am doing something, I can keep my thoughts on it.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
8	Physically I can take on a lot.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
9	I dread having to do things.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
10	I think I do very little in a day.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
11	I can concentrate well.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
12	I am rested.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
13	It takes a lot of effort to concentrate on things.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
14	Physically I feel I am in a bad condition.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
15	I have a lot of plans.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
16	I tire easily.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
17	I get little done.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
18	I don't feel like doing anything.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
19	My thoughts easily wander.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true
20	Physically I feel I am in an excellent condition.	yes, that is true	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	no, that is not true