The Association between Fatigue, Anxiety, and Happiness in the Daily Context of Long Covid Patients: An Experience Sampling Study

Master Thesis

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ABSTRACT

Background: While some people recover after an acute covid-19 infection, others continue to experience symptoms which is also known as long covid. Even though mental and physical fatigue are the most common long covid symptoms, little is known about their fluctuations and association over time. Anxiety and happiness are factors that might increase or decrease fatigue, respectively. **Objective**: The aim of the current study was to enhance insights about mental and physical fatigue in long covid and their associations with anxiety and happiness. **Method**: The Experience Sampling Method (ESM) was utilized to capture repeated momentary self-reports about mental and physical fatigue, anxiety, and happiness over 14 consecutive days. The sample consisted of ten Dutch people with long covid who were discharged from hospital due to a covid-19 infection (M_{age} = 60), with equally male (50%) and female (50%) participants. The variables were assessed six times a day by one item each. The data was analyzed by means of Linear Mixed Models (LMM) in SPSS. **Results**: Results showed a strong positive association between mental and physical fatigue over the assessment period (β = .61, p < .001), significant at both the between person (β = .57, p < .001) and within person (β = .49, p < .001) level. Also, strong positive and significant associations were found between mental fatigue and anxiety (β = .58, p < .001) and physical fatigue and anxiety (β = .53, p < .001). Finally, while between mental fatigue and happiness a moderate negative and significant association was found (β = -.48, p < .001), a strong association was found between physical fatigue and happiness (β = -.61, p < .001). **Conclusion**: Fatigue has been shown to be a severe and common symptom in long covid patients. Mental and physical fatigue were strongly correlated, and mental fatigue was both related to average physical fatigue as well as physical fatigue at a particular timepoint. Further, the more fatigued participants felt, the more anxious they were as well. Finally, less fatigue was related with more happiness, indicating that strengthening happiness might prevent or decrease symptoms of fatigue.

TABLE OF CONTENT

1 INTRODUCTION

Fatigue is the most common symptom in long covid and is characterized by an extreme tiredness that results from mental or physical exertion or illness (Lopez-Leon et al., 2021). Research indicates that fatigue is composed of a mental and physical component which constitute two independent factors (Billones, Liwang, Butler, Graves, & Saligan, 2021). Although this distinction has been recognized in other illnesses, this is not the case in long covid so far. Next to fatigue, anxiety is one of the most common mental health complications in long covid (Lopez-Leon et al., 2021). Despite the suggestion that anxiety might contribute to fatigue, the relationship between both variables has not been examined in long covid patients yet (Walters, Stern, & Stephenson, 2019). A possible approach in controlling or buffering against fatigue might be raising happiness levels. Since long covid is a relatively new health complication, little is known about mental and physical fatigue and its association with anxiety and happiness in people with long covid.

1.1 LONG COVID

Since its emergence in Wuhan, China, coronavirus disease 2019 (covid-19) has spread around the world, profoundly affecting the lives and health of people. Globally, the covid-19 virus infected 465 million people and caused 6.06 million deaths[1] (WHO, 2022). While many covid-19 infections resolve within the first four weeks, some people do not make a full recovery. 'Long covid' is a term used to describe somatic and mental symptoms that continue or develop after an acute covid-19 infection. The term long covid includes ongoing symptomatic covid-19, from four to twelve weeks post-infection, and post-covid-19 syndrome, beyond twelve weeks post-infection. The course of recovery does neither appear to be related to the severity of the initial infection nor to a stay in hospital (Aiyegbusi et al., 2021).

[1] As of 21.03.2022

1.2 FATIGUE

Fatigue is the most common symptom of acute and long covid-19 (Lopez-Leon et al., 2021; Pavli, Theodoridou, & Maltezou, 2021). Up to 60% of covid-19 patients report fatigue at 12 months following recovery from the acute infection, whereby there is no relation between fatigue and the severity of the acute stage of covid-19 (Crook, Raza, Nowell, Young, & Edison, 2021). Overall, fatigue is characterized by a subjective, unpleasant, and overwhelming sense of tiredness associated with impaired physical and/or psychological functioning. As a result, fatigue is accompanied by disinterest, lethargy, and feelings of guilt of not being able to fulfill responsibilities, adversely affecting daily functioning and quality of life (Lasseter, 2009).

Fatigue is composed of a mental and physical component. Mental fatigue is characterized by mental tiredness resulting from cognitive or mental work as well as attention and concentration difficulties. In comparison, physical fatigue refers to the difficulty to initiate or sustain muscle activities, physical exhaustion and a lack of energy not relieved by sleep (Billones et al., 2021). Whereas tiredness disappears with rest or sleep, physical fatigue is an intense and persistent feeling (Lasseter, 2009). In other (lung) diseases the differentiation between mental and physical fatigue is recognized. For instance, while Sarcoidosis patients were more mentally than physically fatigued, chronic obstructive pulmonary disease patients (COPD) report being more physically than mentally fatigued (Kahlmann, Moor, & Wijsenbeek, 2020; Lewko, Bidgood, & Garrod, 2009). Despite these findings, the relation between mental and physical fatigue has not been investigated in long covid patients so far. Since the association between the two types of fatigue can differ among clinical populations, their relationship should be studied in long covid to increase insights about fatigue as a long covid symptom and to build a foundation for interventions.

1.3 Fatigue and Anxiety

Anxiety can be defined as a future-oriented mood state that is activated when approached by threatening or dangerous situations such as illness (Chand & Marwaha, 2022; Miloyan, Pachana, & Suddendorf, 2017). It is therefore not surprising that anxiety is one of the most frequent mental health complications in covid-19. For instance, a study by Moayed et al. (2021) found that the mean score of anxiety of 221 patients with a covid-19 infection was at "extremely severe" levels, with a prevalence of 97%. Additionally, approximately a quarter of patients reported anxiety up to six months after the acute phase of long covid (Pavli et al., 2021). Further, a meta-analysis by Lopez-Leon et al. (2021) showed that 2288 people from a sample size of 45896 experienced anxiety three months after hospital discharge. Psychological factors such as the fear of illness, uncertainty about the future, stress from enduring a potential fatal illness, stigma associated with the illness, and social isolation can contribute to anxiety (Uzunova, Pallanti, & Hollander, 2021).

Fatigue and anxiety have been found to be associated in several clinical conditions. For example, studies found a correlation between fatigue and anxiety has been observed in multiple sclerosis (MS) patients (AlSaeed et al., 2022; Łabuz-Roszak, Kubicka-Bączyk, Pierzchała, Machowska-Majchrzak, & Skrzypek, 2012). In line with this, a meta-analysis confirmed the association between cancer-related fatigue and anxiety (Brown & Kroenke, 2009). Despite these findings, the association between anxiety and fatigue has not been examined in long covid yet. However, it has been suggested that fatigue can be influenced by preexisting anxious feelings (Walters et al., 2019). This knowledge gap raises the need to investigate whether anxiety could be a potential contributing factor to fatigue in long covid. Examining their direct association would enable deeper insights into fatigue as a long covid symptom.

1.4 Fatigue and Happiness

Happiness is a positive emotion that might prove beneficial in managing fatigue in long covid. In psychology, two popular conceptions of happiness exist, namely hedonia and eudemonia. While hedonic happiness relates to pleasure and enjoyment, eudemonic happiness is achieved through experiences of purpose and meaning (Henderson, Knight, & Richardson, 2013). Happy and positive feelings have been found to increase resilience, thus acting as a buffer against stressful situations (Steptoe & Wardle, 2005). Moreover, it was shown that good mood can counteract unhappy states of mood disorders such as those involving depression or anxiety (Rowe, Hirsh, & Anderson, 2007). Further, a study by Michel et al. (2021) found that a positive mindfulness intervention was beneficial at reducing fatigue in a work-related context. Finally, it was shown that the induction of positive emotions in the treatment of fibromyalgia patients led to a decrease in the experience of fatigue and to a general increase in mood state, self-efficacy, and positive emotions (Herrero, Garcia-Palacios, Castilla, Molinari, & Botella, 2014). Based on these findings, it might be possible that happiness also proves beneficial in controlling or buffering against long covid fatigue.

1.5 Experience Sampling Method

While between person measurements focus on what happens across a set of individuals, within person measurements target processes that happen within a given individual (Curran & Bauer, 2011). Since interindividual processes can differ significantly from intraindividual ones, previous findings about fatigue that have been collected on a between person level, cannot be simply generalized to a within person level (Fisher, Medaglia, & Jeronimus, 2018). Between person measurements are typically based on one-time questionnaires and imply the assumption of stability over time (Curran & Bauer, 2011). However, research shows that fatigue, anxiety, and happiness can also fluctuate over time (Csikszentmihalyi & Hunter, 2014; Endler & Kocovski, 2001; Wylie, PraSisto, Genova, & DeLuca, 2022). Accordingly, fatigue, anxiety,

and happiness might be better considered as state variables which can vary from one moment to the next. Hence, it is crucial to assess the course of fatigue and its interplay with anxiety and happiness not solely at one point in time, but at multiple timepoints over a certain time frame.

Experience sampling method (ESM) is a structured self-report diary technique that captures mood, symptoms, and behaviors as they occur in in the current moment. The method assesses participants' momentary experiences several times a day over a period of one or more weeks. In this way, researchers can study participants' actual experience as it occurs in real life. Hence, ESM is employed to investigate experiences within, and in interaction with, participants' everyday environments (Myin-Germeys et al., 2018).

The present study chose this method because of two main reasons. First, existing research on long covid symptoms such as fatigue and anxiety has focused on measuring these concepts at one point in time, neglecting to take the natural flow of real life into account. ESM provides a solution in that it assesses within person variations and enables a deeper understanding of the variability of psychological concepts, thus improving ecological validity (Myin-Germeys & Kuppens, 2021). Second, by studying experiences in the current moment, ESM overcomes the problem of retrospective recall bias. The period in which participants have to recall certain aspects is shorter than in other methods and so the accuracy of information gets improved (Myin-Germeys & Kuppens, 2021).

1.6 Current Study

The aim of the current study was to provide insights into the course and interplay of the long covid symptoms mental and physical fatigue on a momentary level over time. Additionally, it was explored how long covid patients experience anxiety and happiness in relation to fatigue. ESM was used to collect data in form of self-reports about mental and physical fatigue, anxiety, and happiness in people with long covid over the timespan of 14 days.

A study duration of two weeks is recommended for ESM studies since it results in a good response rate of questionnaires (Van Berkel, Ferreira, & Kostakos, 2017).

The following research questions are addressed:

MENTAL AND PHYSICAL FATIGUE

1) How do mental and physical fatigue develop over time and across participants?
2) How are mental and physical fatigue associated in long covid patients over two weeks?
3) Does the association between mental and physical fatigue differ when comparing between persons and within persons over time in long covid patients?

ANXIETY AND MENTAL AND PHYSICAL FATIGUE

4) How is anxiety associated with mental fatigue in long-covid patients over two weeks?
5) How is anxiety associated with physical fatigue in long-covid patients over two weeks?

HAPPINESS AND MENTAL AND PHYSICAL FATIGUE

6) How is happiness associated with mental fatigue in long covid patients over two weeks?
7) How is happiness associated with physical fatigue in long covid patients over two weeks?

2 METHODS

The current study was part of a more extensive ongoing longitudinal cohort study investigating patients' health status after covid-19 hospital discharge from the hospitals Medisch Spectrum Twente (MST; Enschede) and Ziekenhuis Groep Twente (ZGT; Almelo and Hengelo). Patients were asked to fill out a baseline questionnaire directly, three months, six months, nine months, and twelve months after hospital discharge to investigate the long-term consequences of covid-19. An in-depth study was built on this data, consisting of interviews and ESM measurements. The present study solely used data from the ESM measurements.

2.1 PARTICIPANTS

Participants were released from hospital between September 2020 and February 2021. Inclusion criteria for the interview study comprised a) discharge from hospital after PCR-confirmed acute covid-19, b) at least 18 years of age, c) Dutch proficiency. Participants who reported at three months after hospital discharge that their health was significantly better (n=8) or significantly worse (n=16) compared to one year ago were invited to take part in interviews.

In the interviews it was assessed whether participants were suitable for the ESM study. Inclusion criteria encompassed a continued severe impact by (potentially) fluctuating symptoms that could be (primarily) attributed to long covid syndrome or a lack of recovery from covid-19. Based on this, out of the 24 participants, 11 were eligible for the ESM study. However, one participant answered less than 30% of the ESM questionnaires and was therefore excluded from the study. Thus, the final sample consisted of 10 participants, including 5 men and 5 women. Since each participant began the ESM study after being interviewed, all had different starting timepoints and assessment periods. See Table 1 for a full overview of the final sample.

Table 1

Demographical characteristics of the sample

Variables	Category	All participants (N = 10)
Age, M (SD)	Years	59.7 (7.65)
Gender, n (%)	Female Male	5 (50%) 5 (50%)
Education, n (%)	LBO to MBO HAVO to WO	6 (60%) 4 (40%)
Comorbidity, n (%)	No comorbidity One or more comorbidity	2 (20%) 8 (80%)

Note: LBO = lower vocational education; MBO = secondary vocational education; HAVO = higher general education; WO = university

2.2 DESIGN

The present study made use of an exploratory ESM study design in which multiple measures of the same variables were collected over fourteen consecutive days. The daily survey contained two types of questionnaires: The first questionnaire assessing sleep quality was sent once a day at 8 am and was accessible until 12 pm. The second questionnaire contained 21 questions regarding symptoms, mood, and behaviour and was administered six times a day between 8 am and 8 pm. This questionnaire was administered in form of a *signal contingent design*, meaning that notifications to complete the questionnaires were sent at unpredictable times within equal two-hour time intervals. Since the sample group consisted of ill patients, the participant burden was lowered in terms that the questionnaires expired after 15 minutes. The ESM study was conducted via the online research platform *Ethica* which runs on Android and iOS mobile devices. The Ethica questionnaire was pilot tested by the researchers as well as three students with long covid symptoms.

The study was approved by the ethical committee of the BMS faculty of the University of Twente, Enschede (request 210799).

2.3 MATERIALS

The first questionnaire contained six questions assessing participants health and sleep quality, retrospectively. The second questionnaire captured participants symptoms, moods, and behaviour and was administered six times a day. Since the present study focused on the variables anxiety, happiness, and fatigue, solely their corresponding items will be outlined. Anxiety was determined by the item "Right now I feel anxious" (Brys et al., 2020; Pallant & Tennant, 2007; Worm-Smeitink et al., 2021). Next, the item "Right now I feel happy" assessed participants happiness levels (Griffiths & Stefanovski, 2019). Finally, the items "At the moment I feel mentally fatigued" and "Right now I feel physically fatigued" related to the variables mental and physical fatigue, respectively (Bentall et al., 1993; Brys et al., 2020; Kroenke et al., 2001; Lenaert et al., 2020). All items were rated on a seven-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The materials were provided in Dutch.

2.4 PROCEDURE

Participants were invited to join the ESM study during the interview. One day before the beginning of the ESM study, participants were asked to download the app and were provided with an identical questionnaire to the actual study questionnaire to get familiar with the functionalities of the app. With the registration in the Ethica app, participants were asked to sign the written informed consent by default, in which anonymity and confidentiality of the data was ensured. As soon as participants consented, they were able to start using the app.

2.5 Data Analysis

The IBM SPSS Statistics software program (version 26) was used to analyze the data. First, descriptive statistics were obtained on the demographic characteristics of the sample, including age, gender, education, and comorbidities. Additionally, several visualizations were created to illustrate the dynamics of the variables. First, for each mental and physical fatigue two graphs were created, showing the mean mental/physical fatigue scores per participant per day as well as per hours of the day. A further graph was generated to demonstrate the mean mental and physical fatigue scores of the sample across all timepoints. Thereupon, two graphs demonstrating mean mental and physical fatigue and happiness as well as mean mental and physical fatigue and anxiety of the sample across all timepoints were created. Finally, in order to obtain a more precise idea of participants' mental and physical fatigue, anxiety, and happiness over time, one participant with representative scores was randomly chosen as an example for further investigation on the individual level.

Linear Mixed Models (LMM) were the statistical method of choice for conducting the analyses. Since the participants received multiple questionnaires a day over a period of 14 consecutive days, the data points were not independent of each other, and the chance of missing assessments was rather high. LMM are suited for this kind of analyses as they can handle dependent data as well as large amount of missing data (Myin-Germeys et al., 2018). The interpretations of the standardized estimates (ß) were based on the common effect size guidelines of Cohen (1988): $r > .50$ indicates a strong effect, $r > .30$ a moderate effect and $r > .10$ a weak effect.

The association between mental and physical fatigue was tested by first transforming both variables into z-scores to receive standardized regression coefficients. Based on this, a LMM with autoregressive repeated covariance type was performed. Participants were chosen as the subjects and the overall timepoints were selected as the repeated measures. Physical

fatigue was chosen to be the fixed covariate and mental fatigue was set to be the dependent variable.

For the third research question, person-mean scores (PM) and person-mean centred scores (PMC) of physical fatigue needed to be calculated by using the aggregate function in SPSS. PM and PMC scores allow for the disaggregation of between person and within person associations, respectively. As a next step, the variables physical fatigue (PM) and physical fatigue (PMC) were standardized. In the LMM mental fatigue was set as the dependent variable and physical fatigue (PM) as well as physical fatigue (PMC) were set as the fixed covariates.

Research questions four to seven were answered by creating standardized regression coefficients for anxiety and happiness. Thereupon, four LMM with the standardized variables were computed. In the first two LMM, first mental fatigue followed by physical fatigue were set as the dependent variables with anxiety as the fixed covariate. In the following two LMM, again alternately mental and physical fatigue were set as the dependent variables and happiness was chosen both times as the fixed covariate. For each of the four analyses, a LMM with autoregressive repeated covariance type was computed. Also, participants were set as the subjects as well as overall timepoints as the repeated measures.

3 RESULTS

3.1 DESCRIPTIVE STATISTICS

The average response rate of answered ESM questionnaires was 61% (*SD* = 20%; range = 31% – 92%). One participant did not meet the required response rate of 30% during the ESM assessment and was therefore excluded from the study. The mean mental fatigue score of the total sample across all timepoints was 4.2 (*SD* = 1.7), and the mean physical fatigue score was 4.9 (*SD* = 1.6). The mean scores for anxiety and happiness were 2.8 (*SD* = 1.9) and 4.2 (*SD* = 1.5), respectively.

3.2 MENTAL AND PHYSICAL FATIGUE IN LONG COVID PATIENTS

Figure 1 visualizes the mean mental fatigue scores per participant per day. As shown, the scores were not stable but fluctuated notably over the 14 different days. For example, participant 8 scored below 3 on day two, whereas he scored 6 on day twelve. Also, participant 6 became increasingly mentally fatigued from day ten up until day 14.

Figure 1

Mean mental fatigue scores per participant per day during the total assessment period

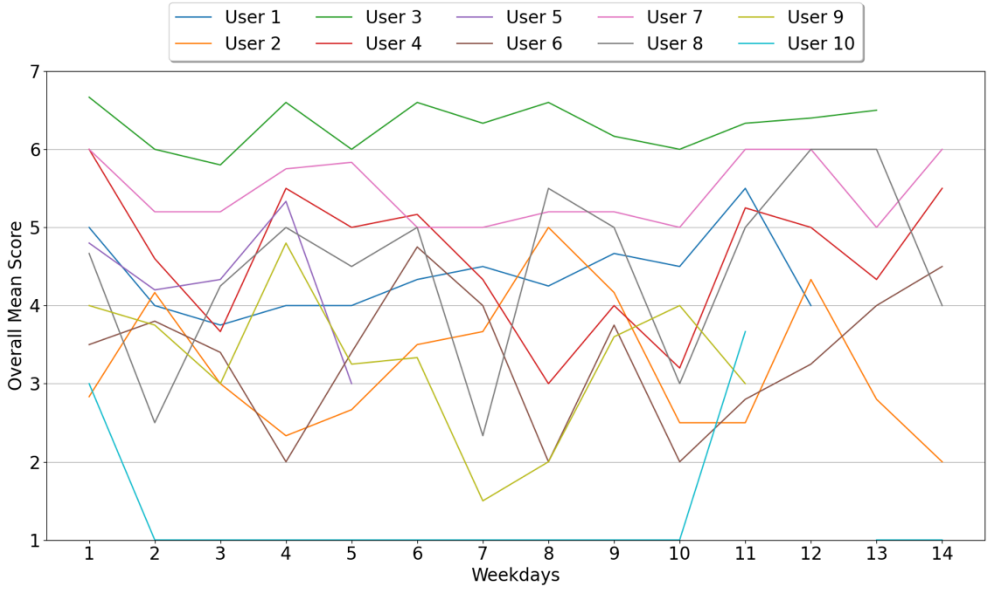


Figure 2

Mean mental fatigue score per participant per hours of the day

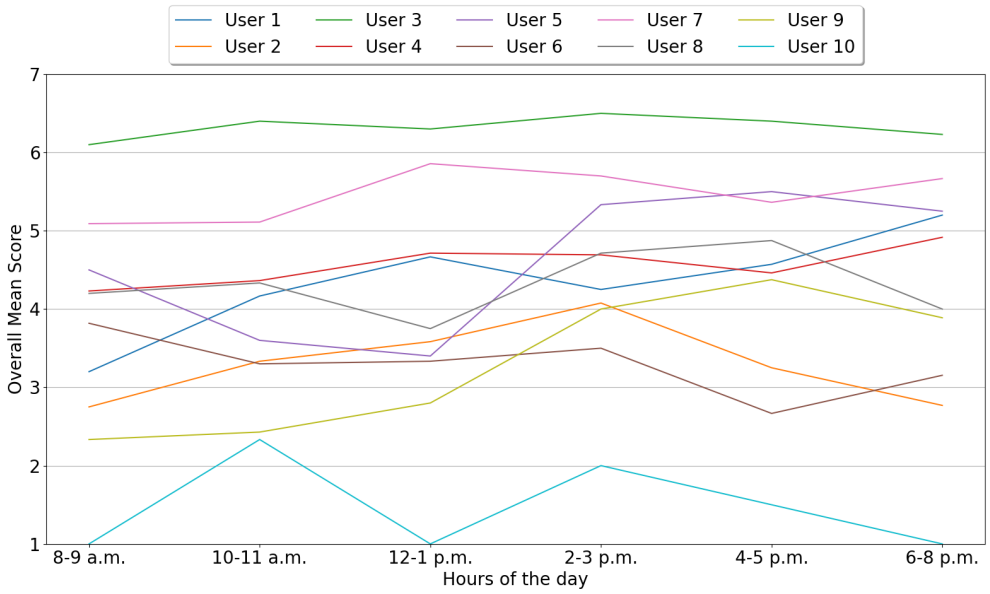
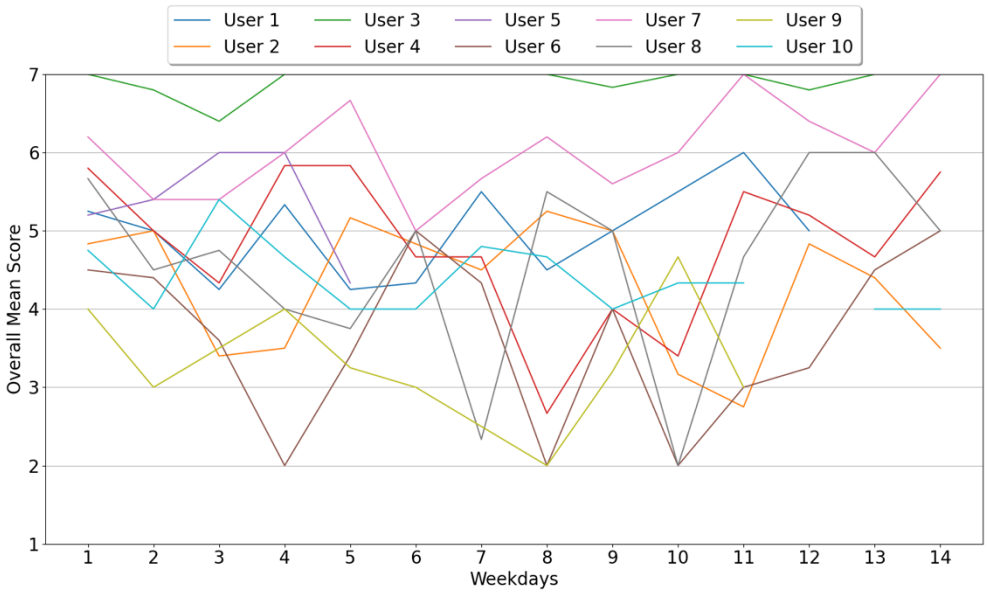


Figure 2 visualizes the mean mental fatigue scores of each participant during a day. Overall, it seems like participants experienced mental fatigue rather consistently. Nevertheless, some participants showed a greater variability and intensity in mental fatigue than others. For instance, participant 9 started an average day with rather little fatigue but then felt increasingly fatigued throughout the day. Around 4-5 p.m. his score reached a peak whereupon it dropped again. Next to this, whereas participant 3 experienced a high intensity in mental fatigue, participant 10 showed low mental fatigue values.

Mean physical fatigue scores per participant per weekday are shown in Figure 3. Again, it can be seen that participants' scores differed considerably from day to day. For instance, participant 6 started the study with a relatively high fatigue score, which then decreased until day four. Thereupon, his physical fatigue score raised and dropped alternately until the end of the study. Figure 4 provides insights about how participants' physical fatigue scores varied throughout an average day. For example, participant 9 felt less fatigued in the morning but got increasingly fatigued until 4 – 5 p.m. as the day passed by.

Figure 3

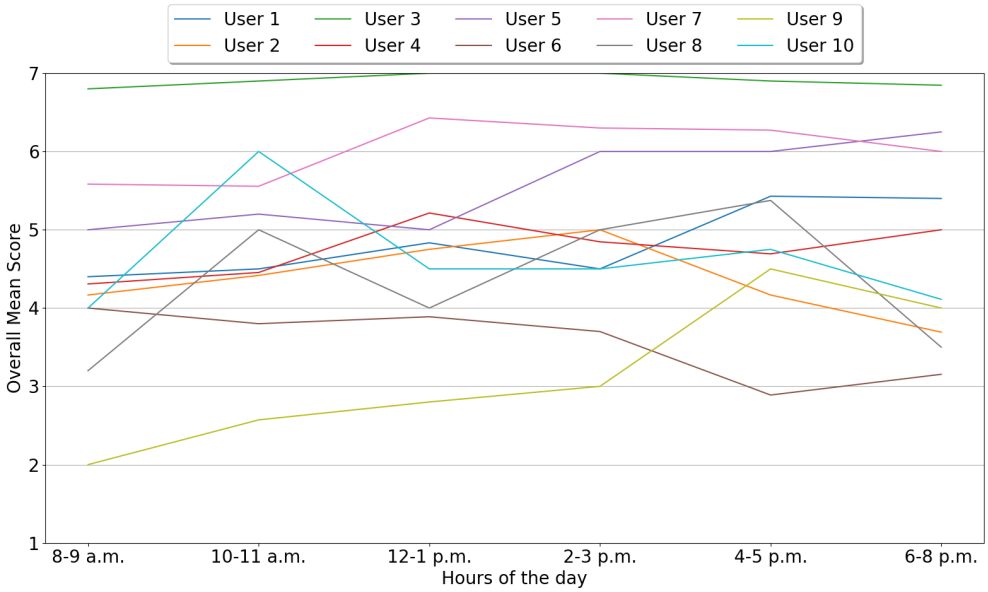
Mean physical fatigue scores per participant per weekday during the total assessment period



Moreover, participant 8 and 10 started off with rather low physical fatigue scores which then increased and reached a peak at 10 – 11 a.m. Afterwards, their scores dropped until a certain time until they increased again. At 4 – 5 p.m. their scores lowered once more, ending the day feeling rather little fatigued.

Figure 4

Mean physical fatigue score per participant per hours of the day



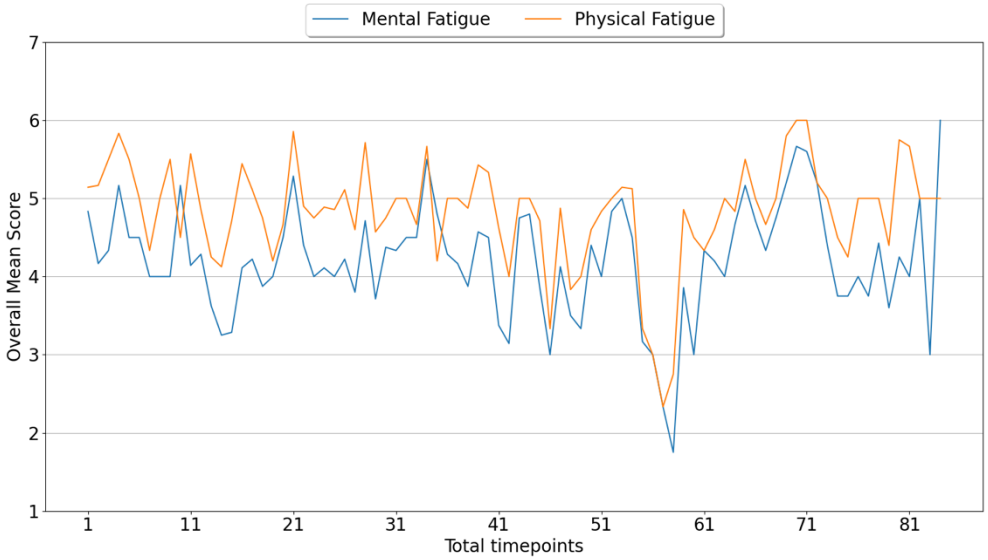
Finally, while participant 3 experienced very high levels of physical fatigue fairly consistently, the scores of participant 2 fluctuated in the moderate range. Like mental fatigue, momentary level scores showed that reported physical fatigue varied significantly both by time of day and day of week.

3.3 Association Between Mental and Physical Fatigue

A LMM was conducted to test the overall momentary association between mental and physical fatigue across all timepoints. Physical fatigue was chosen to be the fixed covariate and mental fatigue was set to be the dependent variable. Results yielded a strongly positive and significant correlation ($\beta = .61$, $SE = .03$, $t(499.30) = 19.53$, $p < .001$, 95% CI [.54, .67]). At the timepoints where participants experienced high or low physical fatigue, they also experienced high or low mental fatigue. Figure 5 shows the group mean scores of both variables across all timepoints.

Figure 5

Mean mental and physical fatigue scores of the sample across all timepoints



3.4 Between and Within Person Associations of Fatigue

A further LMM was conducted to investigate the between and within person associations over time between mental and physical fatigue. In the LMM mental fatigue was set as the dependent variable and physical fatigue (PM) as well as physical fatigue (PMC) were set as the fixed covariates. Results of the LMM yielded a significant and strongly positive between person correlation (β = .57, *SE* = .03, $t(499) = 20.06$, $p < .001$, 95% CI [.51, .62]). When a participant experienced more physical fatigue than another participant in general, they also experienced more mental fatigue than the other person. Further, a significant and moderately positive association was found within persons (β = .49, *SE* = .03, $t(499) = 16.91$, $p < .001$, 95% CI [.43, .55]). When a participant felt more physical fatigued in the current moment, they were also more mentally fatigued than usual. For an overview of the statistical results see Table 2.

Table 2

Between and within person effects of physical fatigue on mental fatigue

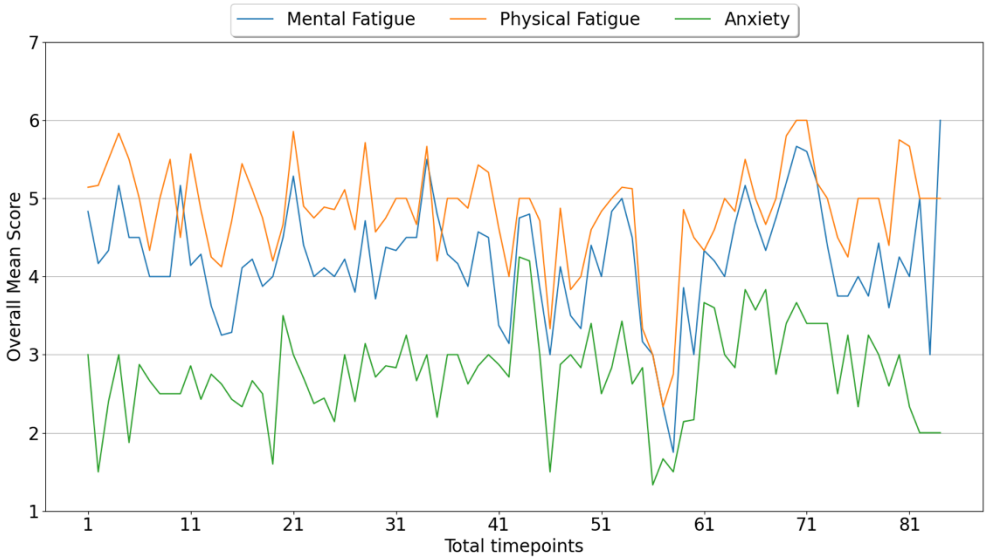
	Standardized ß (95% CI)	t (df)	P
Physical fatigue PM (between person)	.57 (0.51, 0.62)	20.06 (499)	<0.001
Physical fatigue PMC (within person)	.49 (0.43, 0.55)	16.91 (499)	<0.001

3.5 Anxiety and Mental and Physical Fatigue in Long Covid Patients

Two LMMs were utilized to analyze the overall momentary associations between mental fatigue and anxiety as well as between physical fatigue and anxiety across all timepoints. Mental and physical fatigue were set as the dependent variables and anxiety was set as the fixed covariate. First, LMM analysis yielded a strongly positive and significant association between mental fatigue and anxiety ($\beta = .58$, $SE = .05$, $t(121.32) = 11.06$, $p < .001$, 95% CI [.48, .68]). Second, a strongly positive and significant association was found between physical fatigue and anxiety as well ($\beta = .53$, $SE = .05$, $t(135.64) = 10.05$, $p < .001$, 95% CI [.43, .63]). Consequently, when participants experienced more mental or physical fatigue, they were also likely to experience more anxiety at that same moment and vice versa. Figure 6 visualizes the fluctuations of the variables and the positive association between fatigue and anxiety at the group level across all timepoints. It is visible that the fluctuations in mental and physical fatigue over time were associated with fluctuations in anxiety in the same direction. Hence, when mental or physical fatigue increased/decreased, anxiety increased/decreased as well.

Figure 6

Mean anxiety, mental and physical fatigue scores of the sample across all timepoints

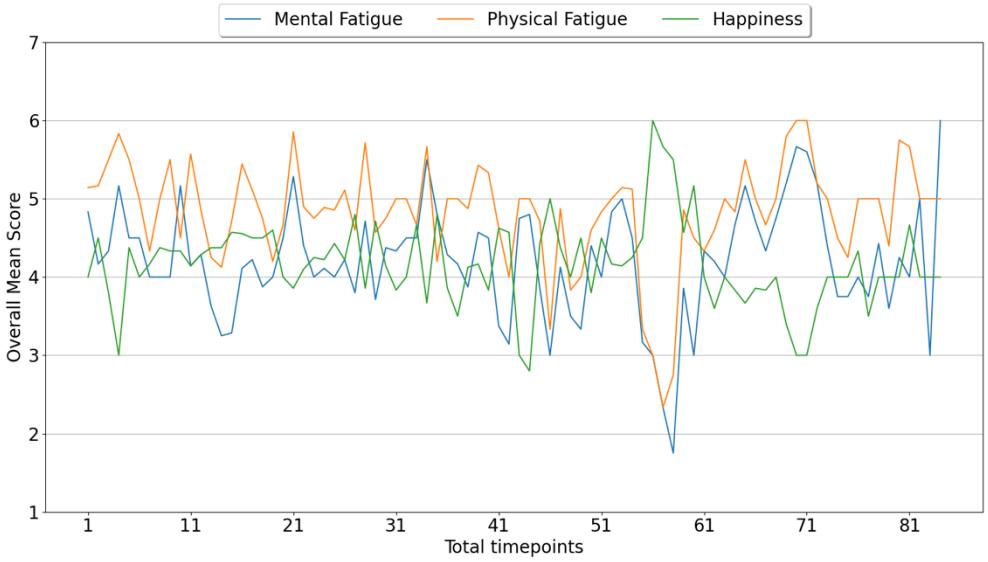


3.6 Happiness and Mental and Physical Fatigue in Long Covid Patients

Two LMMs were conducted to analyze the overall momentary associations between mental fatigue and happiness as well as between physical fatigue and happiness across all timepoints. Mental and physical fatigue were set as the dependent variables and happiness was set as the fixed covariate. Results of the LMMs showed a moderately negative and significant association between mental fatigue and happiness (β = -.48, SE = .05, t(267.47) = -9.53, p < .001, 95% CI [-.58, -.38]) as well as a strongly negative and significant association between physical fatigue and happiness (β = -.61, SE = .04, t(189.06) = -14.12, p < .001, 95% CI [-.70, -.52]). Hence, participants who experienced high mental or physical fatigue tended to experience little happiness at that same moment and vice versa. Figure 7 demonstrates the fluctuations of the variables at the group level across all timepoints. Here, the negative association between fatigue and happiness becomes visible. For instance, while at timepoint 58 mental and physical fatigue were low, happiness was relatively high.

Figure 7

Mean happiness, mental and physical fatigue scores of the sample across all timepoints



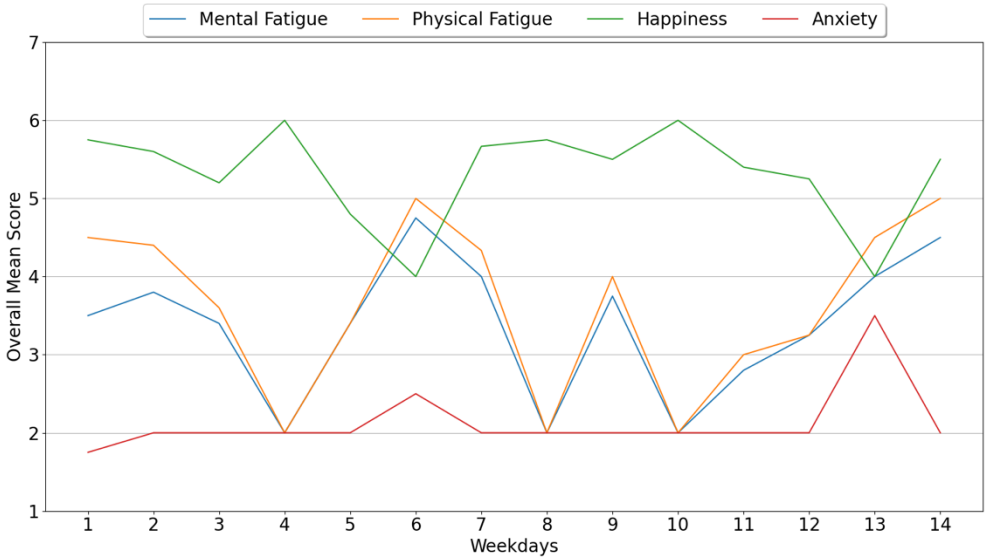
3.7 Individual Case Analysis

A visual case analysis of one participant with representative scores was performed to demonstrate the within person fluctuations and associations between mental and physical fatigue, anxiety, and happiness over 14 days. Visualizations of all participants can be found in Appendix A.

In Figure 8 the average mental and physical fatigue, anxiety, and happiness scores of participant 6 per day are shown. The figure illustrates that all four variables were dynamic and fluctuated from day to day. In general, the participant experienced rather high happiness and rather low anxiety levels. His mental and physical fatigue scores varied in the low to medium range. Additionally, it can be seen that mental and physical fatigue overlapped to a great extent and moved in the same direction, pointing to a positive association on the within person level. Furthermore, a positive association between anxiety and fatigue can be identified. For instance, at timepoint 6 and 13, an increase in fatigue led to an increase in anxiety as well. Finally, the figure demonstrates a negative association between fatigue and happiness.

Figure 8

Mean mental and physical fatigue, happiness, and anxiety scores of participant 6 per weekday



For example, at weekday 4, 6 and 13, it is visible that when there was a drop in fatigue, there was a rise in happiness and vice versa.

This participant was chosen because of the clearly visible within person fluctuations and associations. The individual graphs of all participants can be found in Appendix A. Overall, participants differed in the severity of their variables and the scope of their fluctuations over time. For instance, in contrast to participant 6, participant 7 displayed in general rather low happiness levels with rather high anxiety and fatigue scores. Further, while in participant 6 the variables fluctuated to a great extent, the variables were rather stable in participant 3.

4 DISCUSSION

The purpose of this study was to gain insights into the course and interplay between mental and physical fatigue in long covid patients by using a 14-day Experience Sampling study. Results showed that mental and physical fatigue were common and severe symptoms that varied between and within individuals. Mental and physical fatigue were strongly correlated, and mental fatigue was influenced by both an individual's average level of physical fatigue as well as physical fatigue at a particular timepoint. Moreover, it was shown that high levels of anxiety were associated with high levels of mental and physical fatigue. Finally, the more mentally and physically fatigued participants were, the less happy they felt.

In line with previous studies, descriptive statistics showed that fatigue was a common and severe symptom in this sample of long covid patients (Cares-Marambio et al., 2021; Myin-Germeys & Kuppens, 2021; Raveendran, Jayadevan, & Sashidharan, 2021; Shah, Hillman, Playford, & Hishmeh, 2021; Stengel, Malek, Zipfel, & Goepel, 2021). On average, participants' physical fatigue scores were somewhat higher than their mental fatigue scores which was also found in COPD patients (Lewko et al., 2009). The intensity and fluctuations of mental and physical fatigue differed between and within participants. For instance, while some participants experienced high levels of fatigue rather constantly during a day, others showed fluctuations in the medium range. Overall, the use of ESM illustrated that participants' fatigue levels were not stable but varied significantly during the day and over the total assessment period.

A strong positive and significant association between average mental and physical fatigue was found. On average, the more mentally fatigued patients felt, the more physically fatigued they felt as well. Previous studies on mental and physical fatigue in Parkinson's disease (PD) and MS considered mental and physical fatigue as two independent concepts but did not study their actual relationship (Kahlmann et al., 2020; Lewko et al., 2009). The present study investigated their association and found that both types of fatigue are strongly related. However,

since mental and physical fatigue did not show a perfect association, it is not recommended to consider them as the same concept in long covid.

The aim of the third research question was to explore the association between mental and physical fatigue further by disaggregating the between and within person effects. Fluctuations in physical fatigue over time were associated with fluctuations in mental fatigue in the same direction. Participants with higher physical fatigue scores on average than others also had higher mental fatigue scores at the different timepoints. Additionally, when a person had higher physical fatigue score than his own average, this was associated with a higher mental fatigue score at that timepoint. Since interindividual measurements can differ from intraindividual ones, it was not clear beforehand that a within person effect would be found (Fisher et al., 2018).

The results can find valuable application in interventions targeting fatigue in long covid patients as they suggest that mental and physical fatigue fluctuate over time within individuals. Just-in-the-Moment Adaptive Interventions (JITAIs) are a relatively new type of intervention that provide tailored support at the exact moment of need. Through sensors that are implemented in technologies such as smartwatches, JITAIs can detect changing experiences of individuals and automatically send tailored messages regarding affective states (Wang & Miller, 2020). Therefore, JITAIs might be suitable for targeting fatigue as levels of fatigue show daily fluctuations. Furthermore, individuals can choose whether they would like the intervention to focus on the mental or physical aspect of fatigue. Thus, it is possible to tailor the interventions to different kinds of needs.

People who experienced high levels of mental and physical fatigue were also likely to experience high levels of anxiety. These results are in line with a previous studies which found that fatigue was positively correlated with anxiety in MS patients (AlSaeed et al., 2022; Łabuz-Roszak et al., 2012). Also, a systematic review on cancer-related fatigue showed that anxiety was significantly associated with fatigue (Brown & Kroenke, 2009). This study adds that

anxiety is also a prominent correlate of mental and physical fatigue in long covid. Additionally, both anxiety and mental and physical fatigue move in the same direction over time. Despite this finding, the mechanisms behind the relationship of fatigue and anxiety as well as the question of causality remain uncertain.

This study assessed anxiety as one factor and did not differentiate between the cognitive and somatic components of anxiety. While cognitive anxiety relates to worries, negative expectations, and concerns about oneself, the current situation, and the future, somatic anxiety is characterized by the perception about one's physiological arousal (Beck, Epstein, Brown, & Steer, 1988). This two-factor structure has been supported by a robust body of research, in younger and older populations alike (Smith, Smoll, & Schutz, 1990). Differentiating between the cognitive and somatic dimension of anxiety might provide a more detailed view about which type of anxiety is more prevalent in long covid patients. Also, since anxiety was solely assessed by one single item, it might be that somatic and cognitive anxiety are differently associated with fatigue which would also imply different tailored intervention approaches.

Finally, this study found that when people experienced high levels of mental or physical fatigue, they were likely to experience low levels of happiness. In line with this, COPD patients reported a loss of joy in life due to fatigue (Kouijzer, Brusse-Keizer, & Bode, 2018). The finding indicates that patients perceive long covid fatigue as a factor that contributes to their reduced happiness. Thus, interventions targeting happiness in long covid might prove beneficial in managing fatigue. For instance, the Fordyce Happiness Model (FHM) provides an approach to rebuild and train happiness. The FHM consists of eight cognitive principles and six behavioral principles which comprise removal of concerns, development of a healthy personality, being the real self, lowering of expectations, and priority of happiness (Schrank, Brownell, Tylee, & Slade, 2014). A previous study found that the FHM was effective in reducing fatigue in MS patients after three months (Khayeri, Rabiei, Shamsalinia, & Masoudi, 2016). Thus,

supplementary therapies that focus on increasing happiness, such as the FHM, might also diminish levels of fatigue in long covid.

Even though a significant and negative association has been found between mental and physical fatigue and happiness, it is not clear yet how exactly both variables interact with one another, and which kind of effect happiness exerts on fatigue. For instance, high levels of happiness could lead to a better control of fatigue or could buffer against fatigue right from the beginning. It might also be that the association between happiness and fatigue is mediated by a third factor such as perceived stress, sleep, or daily activities. Thus, further research could test if the association between fatigue and happiness is a causal one or is mediated by a further variable. A combination of qualitative and quantitative methods could potentially offer deeper insights into the effect of happiness on fatigue.

4.1 Strengths, Limitations And Future Direction

The present study contains several strengths which might serve as criteria for further research. First, since Covid-19 emerged in December 2019, little research has been conducted on mental and physical fatigue and their association in long covid patients so far. Therefore, this study offered new insights into mental and physical fatigue as well as their interaction with anxiety and happiness. Second, ESM allowed to assess the variables as they occur in daily life by letting participants answer momentary questions several times a day over 14 consecutive days. This method enabled to capture the variability and associations of fatigue, anxiety, and happiness over time. Since participants completed the questionnaires in real time, the retrospective recall bias was reduced, and the study's ecological validity was improved.

Next to the strengths, the study also faces potential limitations that restrict its validity. First, no disaggregated between and within person correlation analyses of fatigue and anxiety as well as fatigue and happiness were carried out. In a future study, it would be beneficial to differentiate the between and within person effects to ensure that possible fluctuations within

individuals are not overlooked. Second, due to the small sample size of ten participants, it was not possible to distinguish between certain fatigue groups such as men and women. However, factors such as gender or age might be of relevance when studying fatigue (Wylie et al., 2022). Consequently, in future studies larger samples are needed to differentiate between groups and make the findings more generalizable to the larger population (Van Berkel et al., 2017). Finally, solely single items were used to assess the variables. Even though the items were used in previous ESM studies, further items could have increased the reliability and validity of the questions. However, one needs to be careful with not including too many items as this increases the participant burden and might lead to a lower response rate (Van Berkel et al., 2017)

The results revealed that mental and physical fatigue varied within and between participants over the course of the assessment period. In other words, long covid patients experienced different fluctuations and intensities of fatigue, indicating that several subgroups with long covid exist. For instance, a study by Williams, Chalder, Sharpe, & White (2017) suggested that chronic fatigue syndrome is composed of five subgroups, thus supporting a heterogeneous condition. Hence, it might be that certain factors contribute to different experiences of fatigue (Wylie et al., 2022). An interview study might be a way to explore potential underlying characteristics that make a difference in how people experience fatigue. Based on this, factor analysis can be used as a statistical analysis to investigate potential subgroups.

In this study significant associations between mental and physical fatigue, fatigue and anxiety as well as fatigue and happiness were found. However, since only correlational analyses were conducted, no conclusions about causality can be drawn. For instance, it is unknown whether fatigue and anxiety mutually influence one another. Each could be both a cause and an effect of the other. Thus, further research should examine the causality using experimental study designs or cross-lagged panel analyses. This would enable a greater understanding of the variables and could lead to even better intervention approaches.

In conclusion, this ESM study showed that fatigue was a severe and common symptom in long covid patients. Further, mental and physical fatigue varied between and within individuals over time. Mental and physical fatigue were strongly correlated, and mental fatigue was both related to average physical fatigue as well as physical fatigue at a particular timepoint. Furthermore, it was found that the higher the fatigue levels, the higher the anxiety levels were as well. Finally, the more fatigued participants felt, the less happy they were. Further research is needed to properly investigate the associations in a more diverse sample.

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APPENDIX A

In the following, the mean mental and physical fatigue, happiness, and anxiety scores of each participant per day are shown.

Figure 9

Mean mental and physical fatigue, happiness, and anxiety scores of participant 1 per day

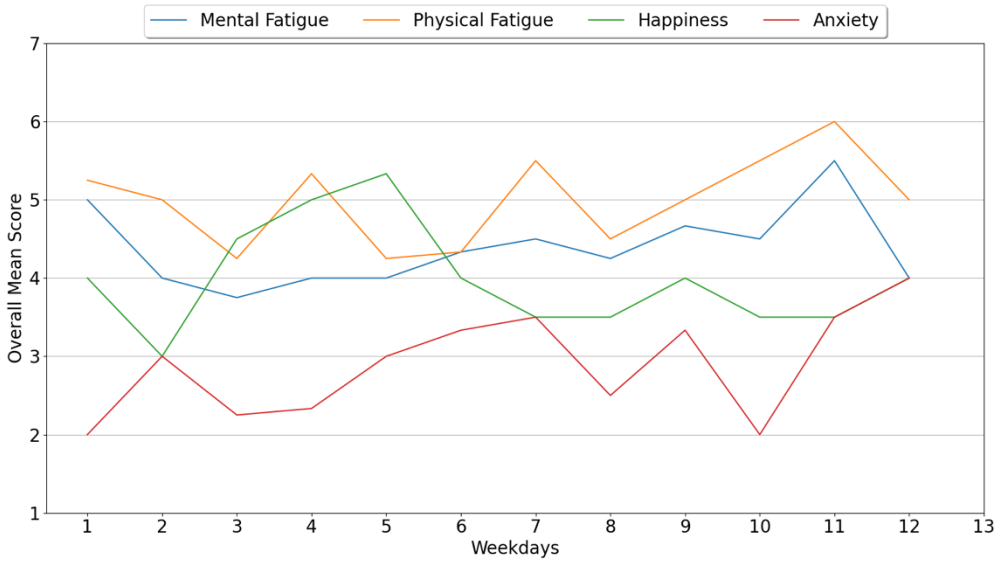


Figure 10

Mean mental and physical fatigue, happiness, and anxiety scores of participant 2 per weekday

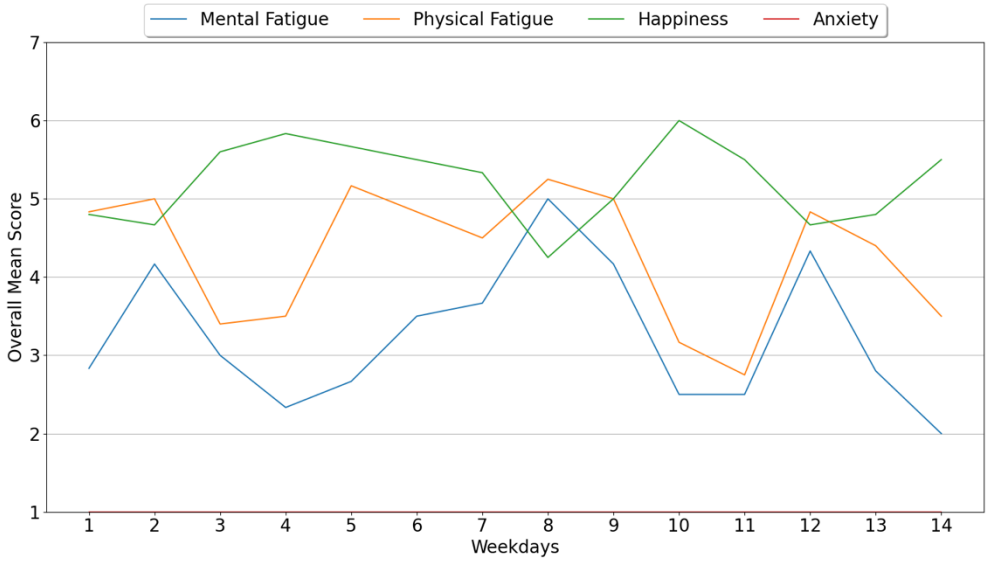


Figure 11

Mean mental and physical fatigue, happiness, and anxiety scores of participant 3 per weekday

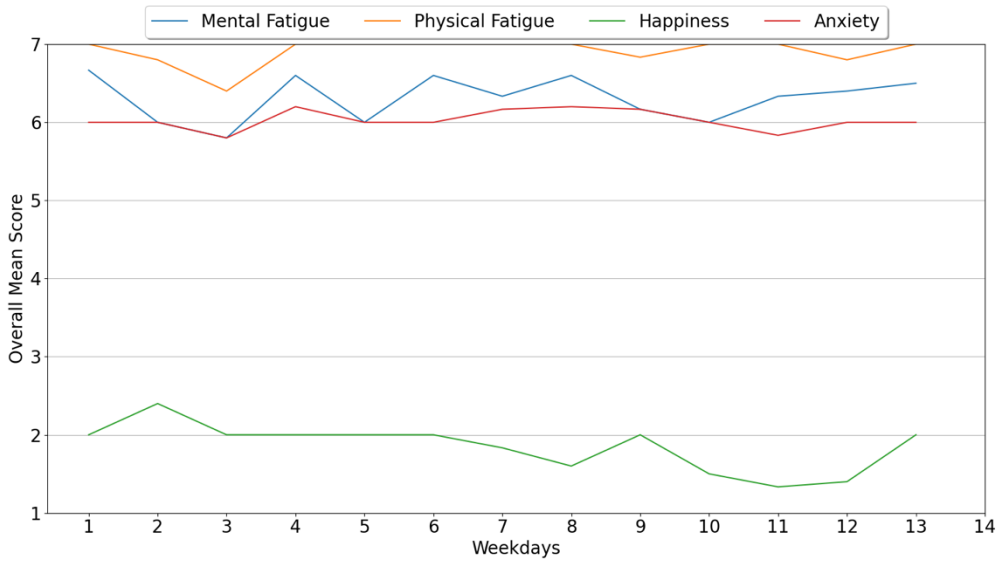


Figure 12

Mean mental and physical fatigue, happiness, and anxiety scores of participant 4 per weekday

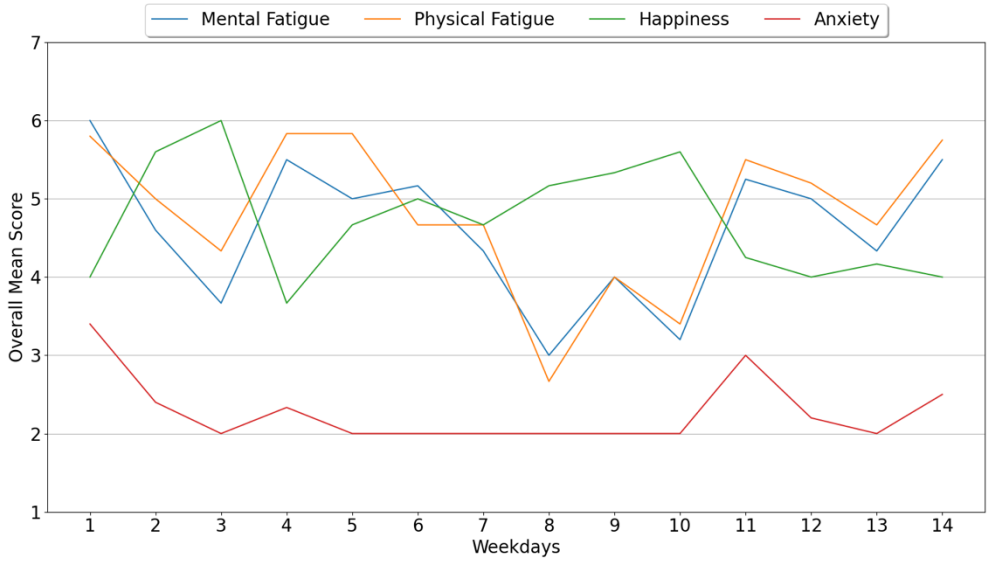
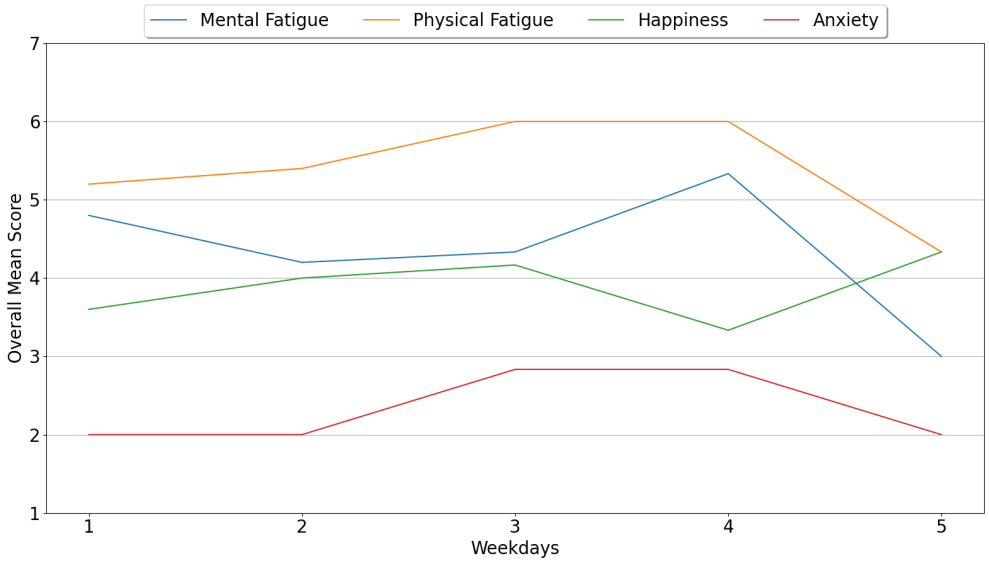


Figure 13

Mean mental and physical fatigue, happiness, and anxiety scores of participant 5 per weekday



Note. This user only participated for five consecutive weekdays

Figure 14

Mean mental and physical fatigue, happiness, and anxiety scores of participant 6 per weekday

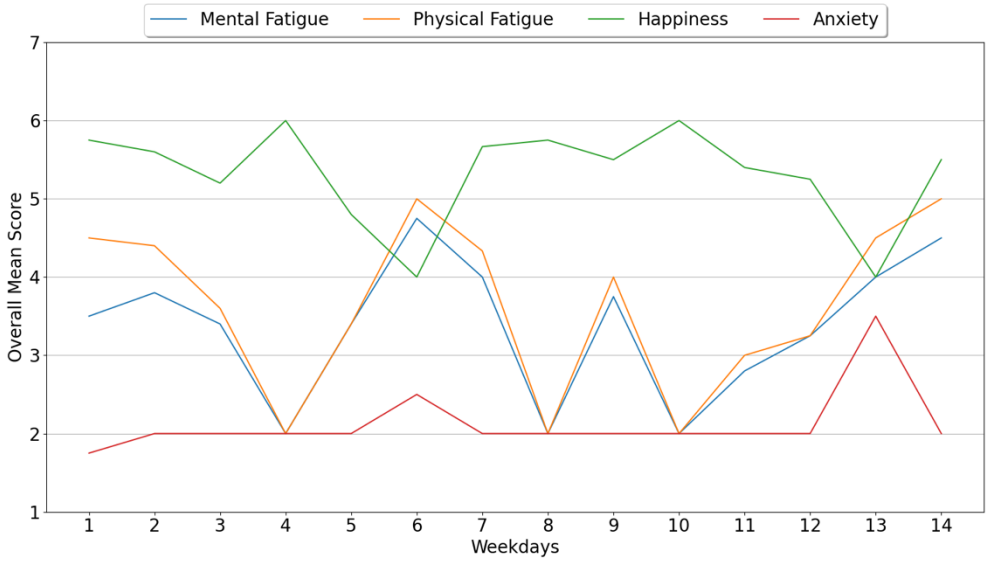


Figure 15

Mean mental and physical fatigue, happiness, and anxiety scores of participant 7 per weekday

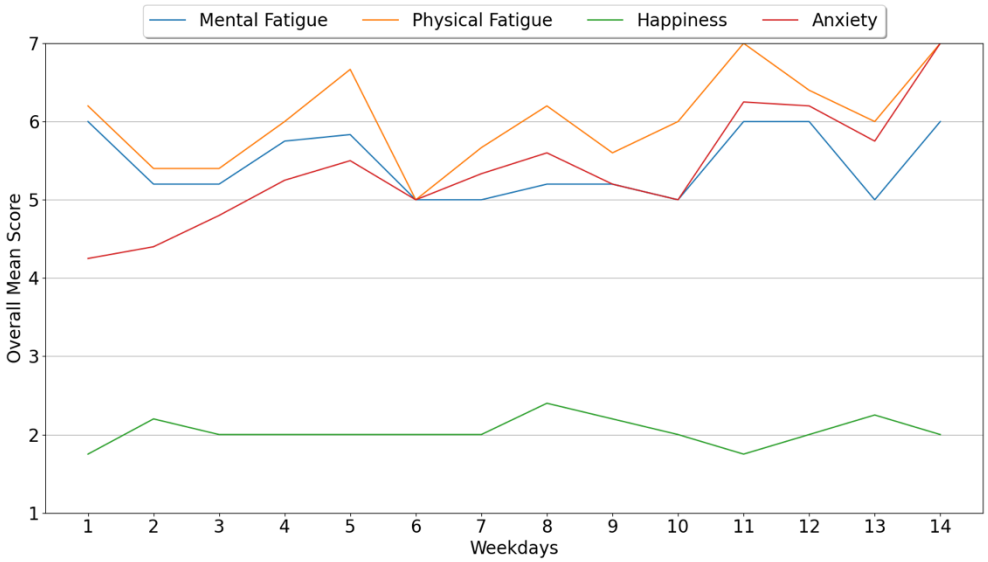


Figure 16

Mean mental and physical fatigue, happiness, and anxiety scores of participant 8 per weekday

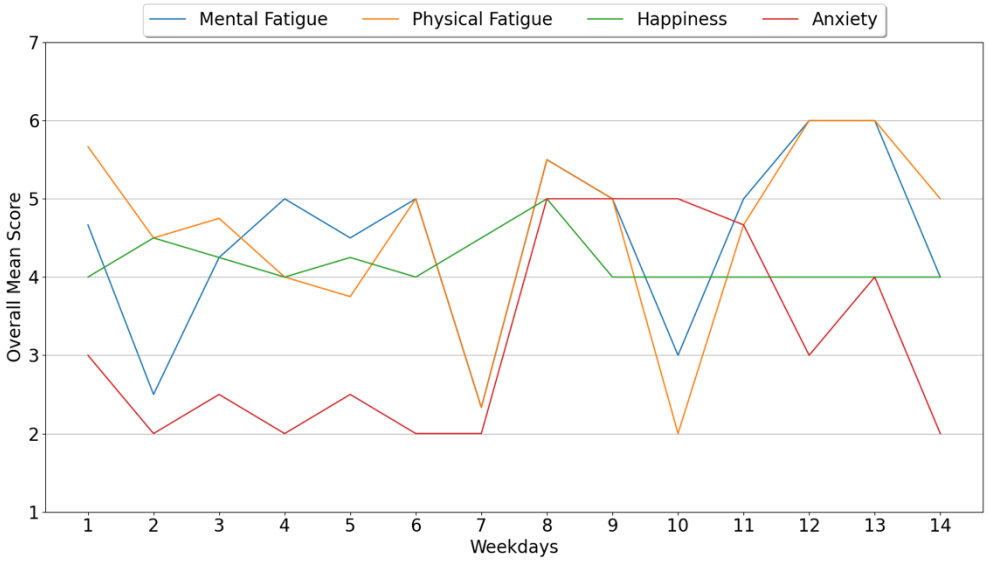


Figure 17

Mean mental and physical fatigue, happiness, and anxiety scores of participant 9 per weekday

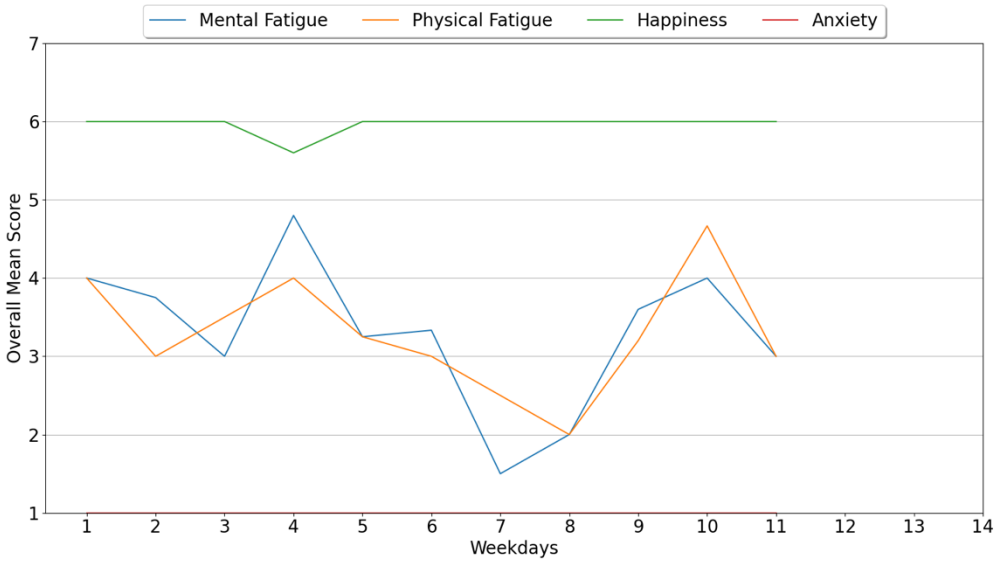


Figure 18

Mean mental and physical fatigue, happiness, and anxiety scores of participant 10 per weekday