The relationship over time between fatigue and subjective well-being in people with Long COVID using Experience Sampling

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Abstract

Background. Following a COVID-19 infection, many people suffer from Long COVID, with the most prevalent symptom being fatigue, mentally and physically. There is very little research on fatigue over time in a daily context and the relationship between fatigue and the experience of positive emotions in patients. Aim. This study sought to fill the knowledge gap and create understanding of the association between fatigue and positive affect, guide future research and potentially give practical advice on optimizing treatment. Methods. Using an Experience Sampling Method (ESM), Dutch Long COVID patients filled in a short survey about mental and physical fatigue and subjective well-being measured as positive affect 7 times a day for 14 consecutive days. The data was analyzed using Linear Mixed Modelling (LMM). The models clarified the relationship of fatigue and well-being in a real-time and real-life environment. Results. There were strong negative associations found between both types of fatigue and positive affect ($\beta = -.19$, p = <.001; $\beta = -.23$, p = <.001). The found associations were much stronger on a between-person ($\beta = -1.18$, p = <.001; $\beta = -1$, p = <.001) than on a within-person level ($\beta = -.2$, p = <.001; $\beta = -.2$, p = <.001). Conclusion. Momentary daily fluctuations in positive affect and fatigue are less associated to each other than the overall levels of the variables. This suggests that individuals with Long COVID who experience fatigue also experience reduced positive affect, highlighting the need for mental health care professionals to pay additional attention to their compromised mental well-being, alongside addressing their physical complaints.

Introduction

Long COVID and health concerns

Since its onset in China, the infectious disease COVID-19 has spread worldwide with over 500.000.000 reported cases and more than 6.000.000 reported deaths (WHO, 2022). The SARS-CoV-2 virus causes a respiratory sickness with the most common symptoms being fever, coughing, shortness of breath, exhaustion and a loss of taste. While most courses of the disease end symptom-free within a couple of weeks, there is a chronicity to the illness that is widely overseen by most literature, which is understandably focusing on the acute treatment and containment of the disease (Marshall, 2020).

Eighty percent of covid survivors suffer from a certain degree of chronicity with at least one typical long-term symptom according to a meta-analysis by Lopez-Leon and her colleagues (2021). 'Long COVID' is a collective term describing a wide range of symptoms, exceeding a regular cause of disease with the most prevalent symptoms being fatigue, headache, attention disorder, hair loss and shortness of breath. The onset of Long COVID is furthermore unrelated to symptom severity with health care professionals reporting chronic symptoms in many moderate and mild causes of COVID-19 patients (Rubin, 2020). These numbers are concerning, considering the estimation that nearly half of the global population has been infected (Barber et al., 2022). Consequently, the prevalence of Long COVID cases is expected to increase as well. Even if most cases of Long COVID are of very mild nature, an ongoing chronification of COVID-19 in the society seeks the attention of a wide range of specialists including 'psychologists, pneumologists, neurologists and specialists in physical medicine and rehabilitation' (Davido et al., 2020).

Fatigue and well-being in Long Covid

Acute and Long COVID have a lot in common with other chronic lung diseases, with fatigue being the most prevalent symptom among multiple diagnoses like chronic obstructive pulmonary disease (COPD) (Baghai-Ravary et al., 2009), chronic bronchitis and emphysema

(Kinsman et al., 1983) and lung cancer (Carnio et al., 2016). Fatigue describes mainly two different phenomena:

- There is physical fatigue, which is defined by Norten et al. (2015) as "debilitating physical exhaustion or a distressing lack of energy not relieved by sleep or rest".
 Elsais et al. (2013) define physical fatigue as muscle fatigue, which inhibits muscle activity.
- 2) The second phenomenon is mental fatigue which is defined by Papakokkinou et al. (2015) as "mental exhaustion that appears especially during sensory stimulation or following mentally strenuous tasks". Typical symptoms are reduced mental capacities, becoming fatigued quickly when engaging in mental activities, extended periods of rest needed to recover from mental activity and becoming more forgetful (Berginström et al., 2017)

Van Herck and his colleagues (2021) found in their longitudinal study that both mental and physical fatigue were highly prevalent over time among members of online Long COVID support groups.

While the symptoms of fatigue can have major implications for the individual's daily functioning, fatigue is also associated with a low positive affect (Krupp, 2003) in multiple sclerosis patients. This association has not yet been investigated in the context of chronic lung diseases, specifically in Long COVID. However, it is an association that warrants analysis, as patients experiencing fatigue may also require the support and attention of mental health care professionals to address potential complaints. Positive affect plays a crucial role in subjective well-being, as emphasized by Diener (2000).

Positive affect

Positive affect can be defined as feelings that are associated to a pleasurable engagement with an individual's environment (Clark et al., 1989). Feelings of positive affect are joy, excitement, happiness, enthusiasm and contentment. Maher and his colleagues (2021) found that there is indication that these feelings were hampered during the pandemic due to the restraints that governments put on the population to slow down the spread of COVID-19.

If positive affect is also associated with fatigue, positive affect might be a concern in Long COVID. Positive affect is not only a fundamental component of subjective well-being. It is also associated with many health-related outcomes as shown by Cohen and Pressman (2005): Positive affect benefits overall mortality, leads to less reported symptoms, increased release of the SIgA antibodies which protects against respiratory diseases and increases overall pulmonary function.

Between-person and within-person associations between fatigue and positive affect

To understand the association between fatigue and positive affect, it needs to be examined on a group-level as well as an individual level as fatigue and positive affect are constructs that fluctuate within a daily context and are dependent on biological, behavioral, psychological and social variables (Brys et al., 2021; Diener & Emmons, 1984). Participants need to be assessed multiple times to enable analyses that allow to distinct between within-person and between-person associations. Within-person associations would indicate that there are situational or behavioral factors influencing the two variables. Between-person associations would indicate that the two variables are related to each other due to individual differences in overall fatigue and positive affect.

Experience Sampling Method

To measure multiple times a day in real-life and real-time, Experience Sampling Method (ESM) was chosen for this research. In ESM, participants repeatedly answer about a current occurring state instead of summarizing how they felt over a longer period of time in one measurement what rules out recall bias. Another reliability advantage of ESM is that measuring briefly in a daily context minimizes the intrusion by the assessment. Furthermore, the method is highly efficient in measuring a construct within a small sample of study participants (Csikszentmihalyi & Larson, 2014)

Research Questions

How do mental fatigue, physical fatigue and positive affect fluctuate throughout the day among Dutch Long Covid patients with a severe course of illness at least 6 months after hospital discharge?

- 1) How do mental fatigue, physical fatigue and positive affect behave throughout the week among Long Covid patients?
- 2) How do mental fatigue, physical fatigue and positive affect behave throughout a day among Long Covid patients?

Are mental and physical fatigue associated with positive affect throughout the day among Dutch Long Covid patients with a severe course of illness at least 6 months after hospital discharge?

Are mental and physical fatigue on both between-person and within-person level associated with positive affect among Dutch Long Covid patients with a severe course of illness at least 6 months after hospital discharge?

Methods

Participants

Sample selection

The data for this study was derived from the data set by (Wensink et al., 2023). The researchers purposively selected participants from an ongoing cohort study which is focusing on patients' perceived health after being hospitalized from MST for a severe COVID-19 infection. 3 months after hospitalization, the cohort study assessed the patients' self-reported health using the Dutch SF-36 (Aaronson et al., 1998) compared to one year ago, so before the onset of the acute COVID infection and hospitalization. 32 patients scored <25 (much worse than a year ago) on the Dutch SF-36 and were considered as non-recovered and selected for an interview study of Schaap and his colleagues (2022). 24 participants accepted the invitation, out of which another 8 had recovered and 16 were still experiencing health complaints. All non-recovered were selected for the study of Wensink and her colleagues (2023) and 11 were willing to participate. 1 more participant was later excluded from the data analysis due to non-compliance.

Inclusion criteria

To be included into data analysis, participants had to comply to at least 30% of the ESM assessments. General inclusion criteria were a) discharged from hospital after PCR-confirmed acute COVID-19; b) continued severe impact of (potentially) fluctuating symptoms that were attributed by the participant to lack of recovery from SARS-CoV-2 infection; c) in possession of a smartphone and willing to install a measurement app; d) minimum 18 years of age; e) proficient in Dutch; and f) written informed consent before participation.

Table 1

Demographic data	Frequency
Gender	
Male	5
Female	5
Age (years)	
40–49	1
50–59	3
60–69	5
70–79	1
Mean age (SD) years	
59.7 (7.65)	
Body Mass Index (kg/m ²)	
18.5–24.9 (healthy weight)	1
25.0-29.9 (overweight)	5
30.0-39.9 (obesity)	2
>40 (morbid obesity)	2
Education	
Primary school	0
Pre-vocational secondary education	5
Higher general secondary education	1
Pre-university education	0
Intermediate vocational education	1
Higher vocational education	2
University	1
Comorbidities	
None	2
One	5
Two or more	3

Participants' demographical data (N = 10).

Procedure

The study was performed on the Ethica application (Ethica Data, 2020) that participants had downloaded on their smartphones. The application was pilot tested at the University of Twente before the actual study with a student who had been experiencing Long COVID symptoms. When the study was conducted, informed consent was asked twice: Once during the interview and a second time via the Ethica platform when the participants joined the ESM study.

The data collection by Wensink (2022) was performed between the first of September and the fifth of November 2021. Every assessment took 14 days with measurements being taken 7 times every day which is in line with research by Klasnja and his colleagues (2008) who suggested between 5 and 8 assessment moments within one day to keep the users engaged without creating too much of a client burden. Participants were asked to provide information regarding their sleep quality once every day between 8 a.m. and 12 a.m. with a reminder at 10 a.m. The questionnaire regarding symptoms and affect utilized a semirandomized sampling scheme, wherein the 6 assessment moments would each randomly occur within a 2-hour timeframe starting with the interval 8 a.m. till 10 a.m. and ending with 4 p.m. till 6 p.m.

Materials and measures

This questionaire addressed multiple Long COVID related somatic symptoms such as shortness of breath, fatigue and pain. All items were scored using a 7-point Likert scales ranging from (1) *strongly disagree* to (7) *strongly agree*.

Fatigue scales

The items for fatigue that were important for this particular research were based on the PHQ-9 (Kroenke et al., 2001) measuring physical fatigue in one item ('I feel physically exhausted at this moment.') and the Wood Mental Fatigue Inventory (Bentall et al., 1993)

measuring mental fatigue in one item ('I feel mentally exhausted at this moment.'). The selected items from the questionnaires were proven to draw reliable conclusions on weekly and daily fluctuations in fatigue (van Kampen, et al., 2020).

Positive affect scale

The second part of the assessment battery measured the participants' emotional affect, both positive and negative emotional affect on a 7-point Likert scales ranging from (1) *strongly disagree* to (7) *strongly agree*. The three items describing positive affect were *relaxation, happiness* and *satisfaction* ('I feel relaxed at this moment.', 'I feel happy at this moment.', 'I feel satisfied at this moment.') and the scale was scored as means. All items were chosen in accordance with earlier ESM-studies applying affect measures and the scale had excellent internal reliability with a Cronbach's Alpha of .936 for this set of data (Brys et al., 2021; Dietvorst et al., 2021; Maes et al., 2015; Worm-Smeitink et al., 2021).

Data analysis

All analyses were performed using IBM SPSS Statistics 26. To answer the first research question, there were descriptive statistics run and graphs created to illustrate physical and mental fatigue as well as positive affect on a group level per week and per day. There were more graphs created for the individual level except for the illustration per day of the week because there were only two samples per day of the week in every participant. These graphs would have been a representation of a participants' day with very limited research value.

Next, there were person-mean-centered scores (PMC) computed for physical and mental fatigue in order to analyze the association between positive affect and fatigue in a later stage of the analysis. Those reflect the deviation of each participant from their mean score over all time points (Curran & Bauer, 2010) by first calculating each participant's mean score over all time points (PM) for both fatigue variables and later subtracting those from participants' daily scores for each time point. Last, z-scores were computed for positive affect, physical and mental fatigue and all computed PM and PMC scores in order to obtain standardized results.

To answer the second research question, linear mixed modeling (LMM) was applied in SPSS. LMM is most useful in handling data from ESM (Eisele et al., 2021) as it is effective when there are many measurements nested within a single individual. To analyze the association between fatigue and positive affect, there were two LMMs with standardized scores run, one with physical and one with mental fatigue as a covariate. Both models were run with positive affect as dependent variable. To illustrate the outcomes, estimated-marginalmeans were used to create line plots that portrait the association between positive affect and fatigue throughout time.

The third and fourth research question was answered by running another two LMM's. This time, the standardized PMs and PMCs of mental and physical fatigue were used as covariates for both models, still using positive affect as dependent variable. The created models now could distinguish on a between- and within-person associations.

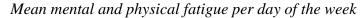
Results

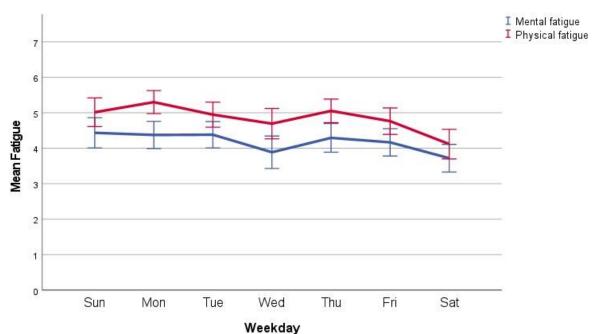
The mean response was 62 (SD = 20) out of 92 assessment moments which equals 60.8% on all measures over time on the three relevant variables which were both mental and physical fatigue as well as positive affect.

Mental and physical fatigue over time

Throughout the week

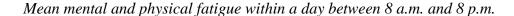
Looking at Figure 1, the means of mental and physical fatigue were plotted per day of the week, representing the whole sample. The mean score for the whole sample on mental fatigue was 4.19 (SD = 1.7) and 4.86 (SD = 1.6) for physical fatigue. The 7 different mean scores representing the weekdays were within the range of one standard deviation for both variables. Both graphs appeared similar to each other indicating an association. Mental and physical fatigue were the lowest on Saturday (M = 3.72; SD = 1.6; M = 4.12; SD = 1.7). Fatigue was highest between Sunday and Tuesday, with physical fatigue peaking on Monday (M = 5.30; SD = 1.5) while mental fatigue was highest on Sunday (M = 5.3; SD = 1.5)

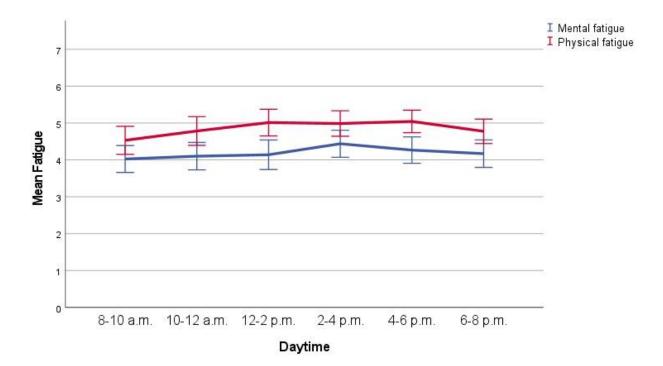




Throughout the day

Figure 2. shows the average fatigue levels between 8 a.m. and 8 p.m. When comparing Figure 1 and Figure 2, fatigue appeared to be stronger dependent on a specific day of the week than on a specific timeslot within one day. The different timeslots in Figure 2 vary only within ¼ of a standard deviation on both fatigue variables which means that a specific time of the day appears to influence fatigue very little. Still, both mental and physical fatigue are represented by a similar pattern in their graphs.

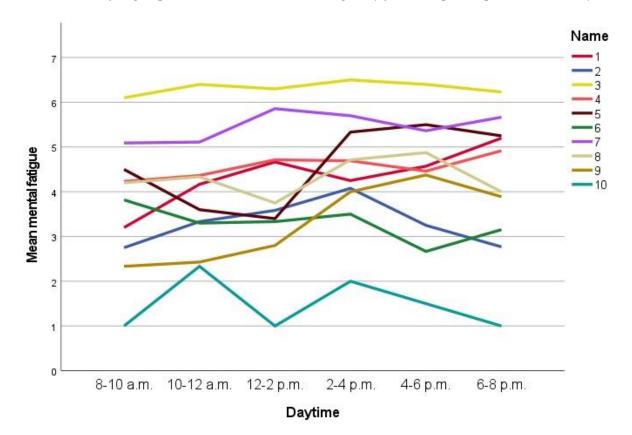




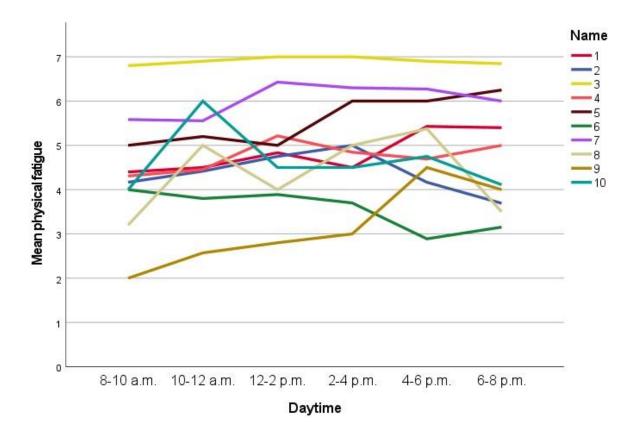
Individual differences in mental and physical fatigue throughout a day

To visualize individual differences, Figures 3 and 4 illustrate mean fatigue per timeslot for all 10 participants individually. Both figures revealed that participants experienced fatigue to a different extent but also in different patterns. The graphs for mental and physical fatigue were similar per individual while they were different to those of other participants, indicating an association between both variables and indicating underlying factors that influence fatigue.

Mean mental fatigue per timeslot within an average day for each participant individually



Mean physical fatigue per timeslot within an average day for each participant individually

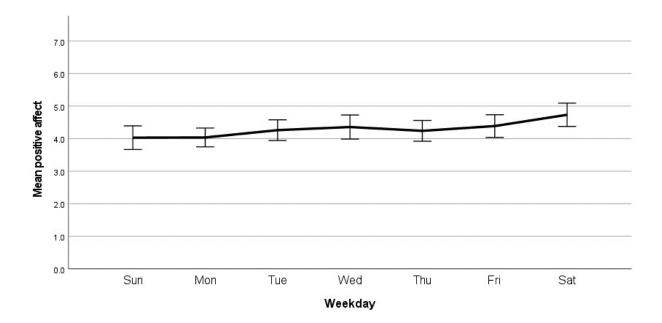


Positive affect over time

Throughout the week

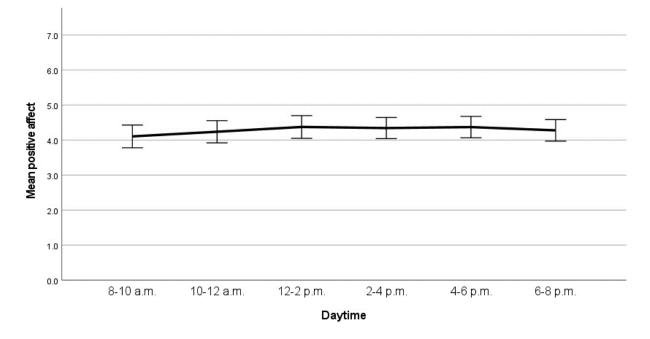
The mean score for the whole sample on positive affect was 4.29 (SD = 1.4). In figure 5, the average positive affect per day of the week was plotted for the whole sample. The different days of the week differed about half a standard deviation in positive affect scores. Positive affect appeard to behave conversely to the two fatigue variables, indicating a negative correlation between positive affect and fatigue. It increased throughout the week with a dip on Thursday (*mean* = 4.24; SD = 1.4) and the peak on Saturday with a mean of 4.74 (SD = 1.5)

Mean positive affect per day of the week



Throughout a day

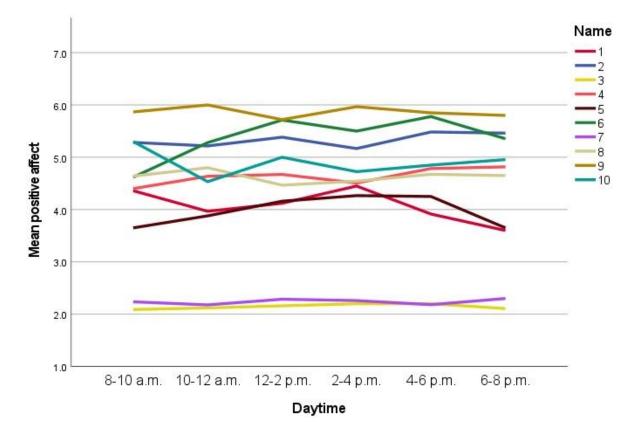
Zooming in on positive affect throughout a day, Figure 6. described a very flat curve. Positive affect was only fluctuating by 0.27 between the highest and the lowest point on average per timeslot in a day among the whole sample, indicating that particular times of the day did not influence the overall experience of positive affect.



Mean positive affect per timeslot within a day

Individual differences in positive affect throughout the day

Moving on to the individual level, Figure 7. shows the average scores on positive affect per participant throughout an average day. Like in fatigue, there were big differences to what extent participants experienced positive affect. Participants who scored high on fatigue tended to score lower on positive affect and vice versa, indicating a negative association between those variables. Individual fluctuations were much bigger in mental and physical fatigue, indicating that the association between and fatigue and positive affect is less due to situational or behavioral circumstances but due to individual differences in the variables.



Mean positive affect per timeslot within an average day for each participant individually

Association between fatigue and positive affect

To answer the second research question, the linear mixed models with standardized zscores revealed that there was as expected a significant negative association between positive affect and both forms fatigue. The full results can be seen in Table 2.

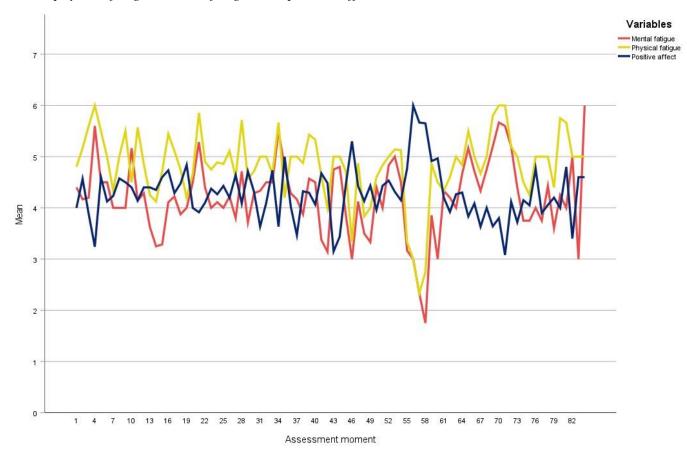
Table 2

LMM analyses with standardized physical fatigue (PF) and mental fatigue (MF) scores as covariates and positive affect as dependent variable

	ß	SE	df	t	Sig.	95% Confid	ence Interval
PF	19	.03	456.79	-7.58	<.001	24	14
MF	23	.03	474.90	-8.01	<.001	29	17

Physical fatigue was negatively associated to positive affect with an estimate of -.19 (SE = .03, p = <.001). The model for mental fatigue and positive affect revealed another negative association of -.23 (SE = .03, p = <.001). Figure 8 depictures that negative association of positive affect and fatigue across the timespan of the study: When positive affect changed, the physical and mental fatigue graphs often changed conversely. This is particularly visible among big fluctuations like the ones between timepoint 56 and 71.

Mean physical fatigue, mental fatigue and positive affect across all timeslots



Between-person and within-person associations of fatigue and positive affect

The outcome of the LMM using PM and PMC scores of physical fatigue as covariate can be seen in Table 3. The model revealed that the two factors were strongly associated on a between-person level ($\beta = -1.18$, SE = .06, p = <.001) indicating that participants who on average suffered from physical fatigue were also very likely to experience less positive affect in comparison to other participants who experience less fatigue. On a within-person level, the two variables were significantly negative associated as well ($\beta = -0.20$, SE = .03, p = <.001) but the association was of small effect size which means that an individual's fluctuations in physical fatigue was little associated with an opposing fluctuation in positive affect.

Table 3

LMM analysis with standardized PM and PMC scores of physical fatigue as covariates and positive affect as dependent variable

	ß	SE	df	t	Sig.	95% Confidence Interval	
ZPM_PF	-1.18	.06	74.56	-21.45	<.001	-1.29	-1.07
ZPMC_PF	-0.20	.03	463.94	-7.25	<.001	26	15

Similar results were found for the second LMM with mental fatigue and positive affect. The corresponding Table 4 shows a much stronger negative association on betweenperson level ($\beta = -1,18$ SE = .11, p = <.001) than on a within-person level ($\beta = -.2$, SE = .03, p = <.001) even though both associations were significant. Like in physical fatigue, a certain baseline of mental fatigue was strong negatively associated to one's positive affect. Fluctuations in mental fatigue in an individual was much less associated with an opposing fluctuation of positive affect.

Table 4

LMM analysis with standardized PM and PMC scores of mental fatigue as covariates and positive affect as dependent variable

	ß	SE	df	t	Sig.	95% Confidence Interval	
ZPM_MF	10	.11	41.26	-9.21	<.001	-1.21	78
ZPMC_MF	20	.03	436.66	-7.07	<.001	26	15

Discussion

This study sought better understanding of the possible association between fatigue and positive affect in Long COVID patients. It was found that there was an association and this association mainly manifested on a level of overall differences in fatigue and positive affect between individuals. This was in line with earlier research by Krupp (2003) among multiple sclerosis patients, although Krupp only researched the overall association, not accounting for situational differences within individuals.

Mental and physical fatigue and positive affect over time

The above-mentioned findings indicate that positive affect must be lower in the Long COVID population compared to other somatic disorders that do not have fatigue as a symptom. This sample experienced indeed less positive affect than other somatic complaints, although generalizability is very limited due to the small sample size: The participants of this sample scored just in between a sample of people with psychological complaints and one with somatic complaints (Maes et al., 2015). There is more research needed to verify that Long COVID patients suffer from reduced positive affect and positive affect might call for special attention in interventions treating Long COVID patients.

Group level

There was no timebound pattern found for either physical or mental fatigue or positive affect throughout the day while other research found that mental fatigue steadily inclines throughout a day in burn-out patients (Söderström et al., 2006).

Comparing the different days of the week, there was a pattern found, although the differences were small. Mental and physical fatigue declined simultaneously throughout the week and positive affect behaved conversely. This was comparable to findings of Stone and his colleagues (2012) who found that positive affect is higher during the weekend which is similar to these results with the exception that Sunday was low on positive affect among this

sample. Long COVID patients who appear to be vulnerable to fatiguing might need special attention within treatment to cope with fatigue, especially throughout the week. Further longitudinal research with a bigger sample is needed to verify the pattern and check for circumstances that explain the potential differences throughout the week.

Individual level

On the individual level, participants appeared to experience fatigue and positive affect with varying severity. Fatigue and positive appeared to be negatively associated when comparing within one individual, already indicating a negative association between them. Mental and physical fatigue appeared to be very similar again. Individuals also varied greatly in times and days, they felt fatigue or positive affect, indicating underlying factors that influence the variables. Physical activity is the factor that is widely mentioned by ESM and general literature to be negatively associated with fatigue, physical fatigue in particular (Maher et al., 2021; Vercoulen et al., 1997; Wensink et al., 2023). Interventions are needed that integrate and test the efficacy of physical activity in the treatment of Long COVID.

Between- and within-person associations of fatigue and positive affect

Participants of this study who experienced more fatigue over time than others, were also very likely to feel less positive affect. Interestingly, this association was much smaller when participants felt different than they would usually do on average. Both fatigue and positive affect fluctuate a lot in a daily context among an individual (Brys et al., 2021; Diener & Emmons, 1984). Finding that the association mostly takes place on average levels of fatigue and positive affect raises the need to understand that association better and this has not yet been discussed by literature. The following paragraph provides a possible explanation.

Causality between fatigue and positive affect

It appears that mental and physical fatigue influence positive affect, as fatigue is a common symptom of not just Long COVID but other respiratory sicknesses as well and

thereby appeared before positive affect (Baghai-Ravary et al., 2009; Carnio et al., 2016; Kinsman et al., 1983). This effect could be explained by physical activity as a mediator between fatigue and positive affect: Research indicated that fatigued individuals tend to avoid physical activity to prevent fatiguing more (Vercoulen et al., 1997). Reduced activity is then also associated with diminished positive affect which indicates that physical activity might be a mediator between fatigue and positive affect (Hong & Dimsdale, 2003).

There is also potential reverse causality, that positive affect influences fatigue: Pressman and Cohen (2005) found that positive affect is negatively associated with symptom sensitivity which implies that participants who feel little positive affect would also experience their symptoms of fatigue as more severe. That would potentially again lead to reduced physical activity, more fatigue and reduced positive affect. This would conclude a negative spiral that could also explain the stronger association between average levels of fatigue and positive affect mediated by physical activity in comparison to situational factors relating the two variables to each other.

More research is necessary to examine causality between fatigue, positive affect and other underlying factors. Factor analysis should be applied to check for underlying factors. To check for causality, a first step could be to use the ESM data of this study for lagged analyses wherein predictions in state differences from one assessment point to the next are tested to test for possible effects.

Another way to test for an effect would be to include manipulations, incorporating multiple interventions targeting fatigue and well-being to analyze what kind of treatments are effective in reducing symptoms and possibly even enhance the recovery process from the disease. Using interventions that incorporate physical activity seem promising as physical activity is not only predicting lower levels of fatigue (Puetz, 2006) but it also has a direct positive influence on well-being (Fox, 1999).

Strengths and limitations

There is limited reliability in drawing conclusions about a overal levels of positive affect and fatigue among Long COVID patients. This sample's average scores drawn from 10 participants is not a reliable representation of the whole Long COVID population and thereby no conclusions or comparisons can be drawn with other populations. These kinds of conclusions still ask for a much bigger sample size.

The descriptives concerning fatigue and positive affect throughout the day contain a lot more samples as there were 14 measurements taken for every timeslot within every individual in comparison to 2 in weekdays. Still, it is an unreliable measure as a very small sample size repeatedly took the assessments, possibly reproducing the same biases due to personal circumstances. Another limitation was the low response rate of 60%. This could be due to multiple reasons.

While this sample is not representative for a whole population, ESM data enables reliable analyses about the nature of associations within a limited sample size. ESM is thereby very cost efficient and enables a distinction between associations on group and individual levels. Traditional approaches assess variables once or twice which makes them vulnerable to recall biases. Individual differences are harder to assess with traditional approaches as states can last shortly and are vulnerable to any kind of intrusion by an assessment. Measuring in real-life and real-life in contrast to traditional methods, enabled high ecological validity.

Conclusion

The goal of this research was to examine the relationship between the most common symptom in Long COVID fatigue and positive affect in a daily context. This study found that positive affect should be evaluated when being confronted with fatigue as a symptom. Both were strong negatively associated with each other. The association was highest on the between subject level, with the possible mediating factor of physical activity. Future research needs to examine that association and possible underlying factors in more detail to maximize the efficiency of treatment.

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