ASSOCIATION BETWEEN LIFESTYLE- AND CIRCADIAN RHYTHM-RELATED CHANGES, AND DIFFERENT DEPRESSION SYMPTOM CLUSTERS DURING COVID-19

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SUMMARY

Background: The COVID-19 pandemic brought along a new situation for the population worldwide. The most important safety measures and lockdown expected extreme adaptability and flexibility impacting mental well-being. The aim of our study was to identify associations between changes in lifestyle and circadian rhythm and depression during the pandemic.

Subjects and methods: Our analysis has been carried out on the Hungarian data set of the COMET-G study including information on lifestyle and circadian rhythm-associated factors and severity of depression and its 3 symptom clusters. Associations were assessed using linear regression models adjusted for age and sex.

Results: All variables reflecting changes in quality and quantity of sleep showed significant associations with overall depression scores and the three distinct symptom cluster scores. All variables reflecting importance and changes in physical activity during the pandemic were similarly significantly associated with all depression measures. However, only changes in quality of diet, but not quantity was associated with depression scores.

Conclusions: Our results may confirm the association of circadian rhythm and lifestyle-related environmental factors in deterioration of mental health during COVID and help devise prevention and intervention methods and targets for similar situations.

Key words: COVID-19 - depression – diet - lifestyle - circadian rhythm - physical activity – sleep

Abbreviations: CES-D - Center for Epidemiologic Studies Depression Scale; Dep-Som – depressive affect and somatic complaints; Irr-Soc – irritability and problems with social relationships; PA – lack of positive affects

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INTRODUCTION

COVID-19 has presented unprecedented obstacles to carrying on with our normal way of living in our society. The emergence of the pandemic affected all parts of the world and had a serious impact not only on somatic, but also on mental health. Furthermore, it has influenced almost all aspects of life, including education, economy, and healthcare, however, the greatest challenge has been experienced by people at the individual level. The appearance of the virus causing a potentially fatal infection and the lack of protection and treatment alternatives created a previously unimaginable life situation. With social distancing, the living space decreased, individuals became isolated, which clearly affected their mental health and lifestyle, including sleep cycle, diet and sport related habits and thus increasing the risk and prevalence of depressive and anxiety symptoms.

A large number of studies show that the COVID-19 pandemic mostly had a negative impact on mental health and different aspects of lifestyles (Fountoulakis et al. 2022, Marano et al. 2021, Yang et al. 2021), however, in some cases a slight positive impact on lifestyle factors during the quarantine was observed, such as a mild increase in physical activity and decrease in the number of smokers (Di Renzo et al. 2020) and also an increase in positive rather than negative feelings (Foa et al. 2020, Recchi et al. 2020), and in the longer term an improvement in mental well-being via post-traumatic growth and resilience (Gonda & Tarazi 2021, Vinkers et al. 2020).

The psychological effects of the pandemic are not negligible, as it is associated with a higher prevalence of mental health symptoms and disorders as well (Cénat et al. 2021, Deng et al. 2021). An early systematic review and meta-analysis reported that 29.6% of the participants experienced stress, while the prevalence of depression was 33.7% and the prevalence of anxiety 31.9% among the general population (Salari et al. 2020). Another systematic review and meta-analysis showed a high prevalence of depression (45%), sleep disturbances (34%) and anxiety (47%) among COVID-19 patients (Deng et al. 2021). Thus, it seems

that the negative psychological effects of the SARS-CoV-2 seriously affect not only the COVID-19 patients, but also those who have to face this worldwide crisis.

The different lifestyle changes resulting from the pandemic and related measures and lockdowns are particularly important because they can affect the presence of mental symptoms or disorders in both a direct or indirect way. Results already show that unhealthy lifestyle habits are more typical during the pandemic (Cervera-Martínez et al. 2021) and beyond their well-known role in the development of mental health symptoms and the deterioration of mental well-being, they also offer intervention and prevention possibilities.

Thus, it is of key importance to understand how lifestyle and circadian-rhythm related factors are affected during the pandemic and the related lockdowns, and also how they are related to different aspects of depression and mood symptoms in part to help prepare for similar situations that may occur in the future. The aim of the current study was to investigate the association between changes in lifestyle and circadian rhythm-related factors including multiple aspects of quality and quantity of sleep, diet and physical activity, and depression specifically focusing on its distinct symptom clusters in a general population during the COVID-19 pandemic.

SUBJECTS AND METHODS

Methods

The present analysis has been carried out on the Hungarian dataset of the COMET-G (COVID-19 MEntal health in Ternational for the General population) study, an international initiative to assess the effects of the COVID-19 pandemic and related lockdown measures on mental health. The collaboration includes 55589 self-selected general population participants from 40 countries, data were collected online and anonymously between April 2020-March 2021. The Hungarian leg of the study was approved by the Regional, Institutional, Scientific and Research Ethics Committee of Semmelweis University and included 763 participants recruited via snow ball method. Besides demographic data participants provided information regarding different aspects of lifestyle and circadian rhythm-associated factors, including their sleep cycle, sport and diet related habits. Variables were interpreted in relation to CES-D scores (Center for Epidemiologic Studies Depression Scale) which allowed the assessment of affective symptoms.

Participants

763 participants (617 women) with an average age of 41.98 (range 18-80 years) were recruited in the Hungarian population. Inclusion criteria only included willing to participate and capacity to complete the online questionnaire, exclusion criteria included intellectual disability, acute psychotic state, being under the influence of alcohol or other psychotropic substances. Participation was voluntary and no compensation or reward of any sort followed. Participants were reached on social media platforms via snowball method. All participants provided informed consent before proceeding to participate in the online study.

Procedure

Data were collected online and anonymously between April 2020-Mach 2021 starting after the regulations and measures as a response to the first wave of the pandemic took effect, covering both periods of full implementation of lockdowns as well as of relaxations of measures.

Measures

Severity of affective symptoms was measured by the Hungarian version of the Center for Epidemological Studies Depression Scale (CES-D). The questionnaire consists of 20 items, each scored on a Likert-scale from 0-3 (including reverse items), with total scores varying between 0-60. CES-D scores were also divided into 3 subscales to capture distinct symptom clusters, focusing on lack of positive affects (CES-D PA) (items: 3, 4, 8, 12, 14, 16), irritability and problems with social relationships (CES-D Irr-Soc) (items: 1, 11, 15, 19) and depressed affect and somatic complaints (CES-D Dep-Som) (items: 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 17, 18, 20) to allow assessment of different manifestations of affective symptoms with potentially different biological and environmental etiological contributors (Fountoulakis et al. 2001). Unless noted otherwise, lifestyle related factors were assessed by a 5 item Likert-scale.

Questions regarding changes in quality and quantity of sleep included "The quality of my sleep has changed recently" (SLEEP1), "I tend to stay up late and sleep for many hours during the day" (SLEEP2), "I take sleeping pills to help me sleep at night" (SLEEP3), and "I am having dreams in which I feel trapped, over the last 3 weeks" (SLEEP4).

Questions focusing on physical activity and its importance and changes during the pandemic included "Does exercise help you in the prevention of anxiety?" (SPORT1), "Do you consider that exercise is important during this pandemic?" (SPORT2), "Do you have increased the frequency and intensity of your physical workout during this pandemic and lockdown?" (SPORT3), and "How much has your physical activity been affected by this epidemic of COVID-19?" (SPORT4).

Questions assessing changes in quality and quantity of diet during the pandemic included "During the days of the lockdown did you notice the need to eat larger amounts of food or eat more often?" (DIET1), "Please mark the answer that best represents you during the period of the lockdown: 1=I eat in a healthier way; 0=My eating habits and preferences have not changed; -1=I eat in a more unhealthy way" (DIET2), "Please mark the answer that best represents you during the period of the lockdown: -2=My body weight has significantly decreased (more than 2-3 kilos); -1=My body weight has slightly decreased (less than 2 kilos lost); 0=My body weight is stable; 1=My body weight has slightly increased (less than 2 kilos put); 2=My body weight has significantly increased (more than 2-3 kilos)" (DIET3).

Statistical analysis

Unadjusted and adjusted (to age and sex) linear regression models were used to assess the effect of each predictor separately after a general graphical assessment. Mean difference associated for each unit of change for continuous or between group differences for categorical predictors and their 95% Confidence Intervals (CI) were calculated. Missing data was not imputed for any variables used in the analysis. Benjamini-Hochberg correction was used to calculate adjusted p-values (FDR q) to account for multiple testing (Storey 2002). The total number of independent test (one for each predictor) conducted was reported. All statistical analyses were performed using STATA version 15.1 (StataCorp 2017).

Table 1. Associations between the overall CES-D score and its three individual factors and quality and changes of sleep cycle during the first two waves of the COVID-19 pandemic

| Sleep cycle	Beta	Std. Err.	t	p	FDR q	95% CI	
SLEEP 1	*CES-D overall*						
The quality of my sleep has changed recently	-5.37	0.39	-13.84	<0.0001	<0.0001*	-6.13	-4.61
	Lack of positive affects (CES-D PA)						
-2=Much worse,	-1.67	0.17	-10.08	<0.0001	<0.0001*	-2	-1.35
-1=A little bit worse,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
0=The same,	-1.11	0.08	-13.32	<0.0001	<0.0001*	-1.28	-0.95
1=A little better,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
2=Much better	-4	0.27	-14.59	<0.0001	<0.0001*	-4.54	-3.46
SLEEP 2	*CES-D overall*						
I tend to stay up late and sleep for many hours during the day	2.40	0.28	8.58	<0.0001	<0.0001*	1.85	2.95
	Lack of positive affects (CES-D PA)						
0=Almost never,	0.69	0.12	5.95	<0.0001	<0.0001*	0.46	0.92
1=Rarely,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
2=Sometimes,	0.41	0.06	6.83	<0.0001	<0.0001*	0.30	0.53
3=Often,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
4=Almost always	1.88	0.20	9.49	<0.0001	<0.0001*	1.49	2.27
SLEEP 3	*CES-D overall*						
I take sleeping pills to help me sleep at night	3.66	0.45	8.08	<0.0001	<0.0001*	2.77	4.55
	Lack of positive affects (CES-D PA)						
0=Almost never,	1	0.19	5.30	<0.0001	<0.0001*	0.63	1.37
1=Rarely,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
2=Sometimes,	0.73	0.10	7.57	<0.0001	<0.0001*	0.54	0.93
3=Often,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
4=Almost always	2.83	0.32	8.82	<0.0001	<0.0001*	2.20	3.46
SLEEP 4	*CES-D overall*						
I am having dreams in which I feel trapped, over the last 3 weeks	5.89	0.70	8.36	<0.0001	<0.0001*	4.51	7.27
	Lack of positive affects (CES-D PA)						
0=Almost never,	1.79	0.29	6.13	<0.0001	<0.0001*	1.22	2.37
1=Rarely,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
2=Sometimes,	1.41	0.15	9.44	<0.0001	<0.0001*	1.11	1.70
3=Often,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
4=Almost always	4.21	0.50	8.35	<0.0001	<0.0001*	3.22	5.19

Note: 95% CI - 95% Confidence interval;   CES-D - Center for Epidemiologic Studies Depression Scale;
Dep-Som – depressive affect and somatic complaints;   PA – lack of positive affects;   Irr-Soc – irritability and problems with social relationships;   * significant results surviving correction for multiple testing (FDR q<0.05)

RESULTS

Associations between changes in quality of sleep cycle during the COVID-19 pandemic and depression and its different symptom clusters

All variables assessing quality and changes in sleep cycle during the pandemic showed a significant association with both the overall CES-D score and its individual factors. Specifically, a positive change in sleep quality was markedly associated with a lower CES-D score (β=-5.37, q<0.0001) as well as lower scores on lack of positive affects (CES-D PA) (β=-1.67, q<0.0001), irritability and problems with social relationships (CES-D Irr-Soc) (β=-1.11, q<0.0001) as well as depressed affects and somatic complaints (CES-D Dep-Som) (β=-4.00, q<0.0001) factors. A higher tendency to stay up late and sleep for many hours

during the day indicating disrupted circadian rhythm was associated with a higher overall CES-D score (β=2.40, q<0.0001) and increased scores on all three individual factors (CES-D PA: β=0.69, q<0.0001; CES-D Irr-Soc: β=0.41, q<0.0001; CES-D Dep-Som: β=1.88, q<0.0001). A higher frequency of taking sleeping pills to help sleep at night was associated with a higher overall CES-D score (β=3.66, q<0.0001) as well as an increase on all three factors (CES-D PA: β=1.00, q<0.0001; CES-D Irr-Soc: β=0.73, q<0.0001; CES-D Dep-Som: β=2.83, q<0.0001). Additionally, an increased frequency of having nightmares in which one feels trapped was associated with an increase on the overall CES-D score (β=5.89, q<0.0001) and all three individual factors (CES-D PA: β=1.79, q<0.0001; CES-D Irr-Soc: β=1.41, q<0.0001; CES-D Dep-Som: β=4.21, q<0.0001) (Figure 1, Table 1).
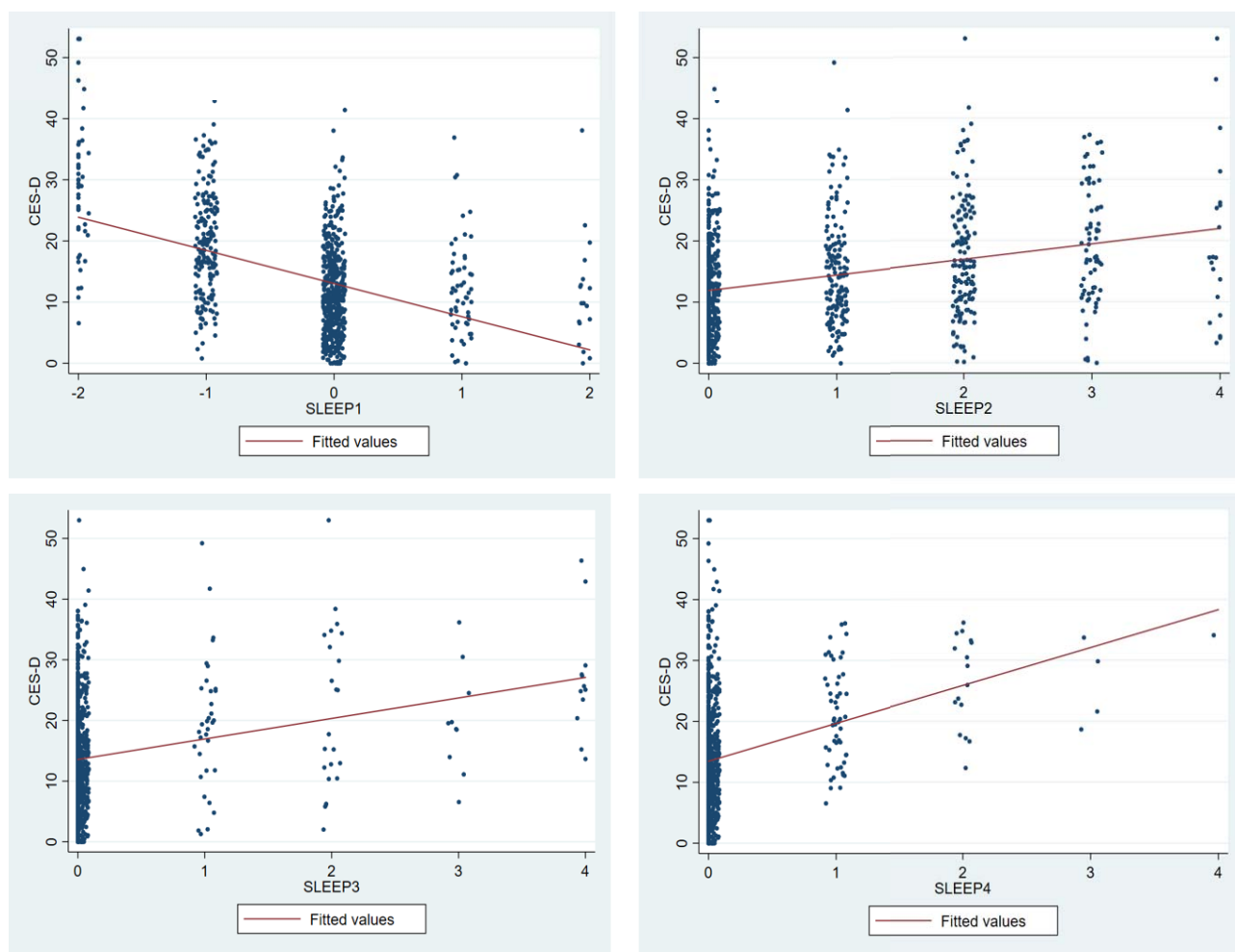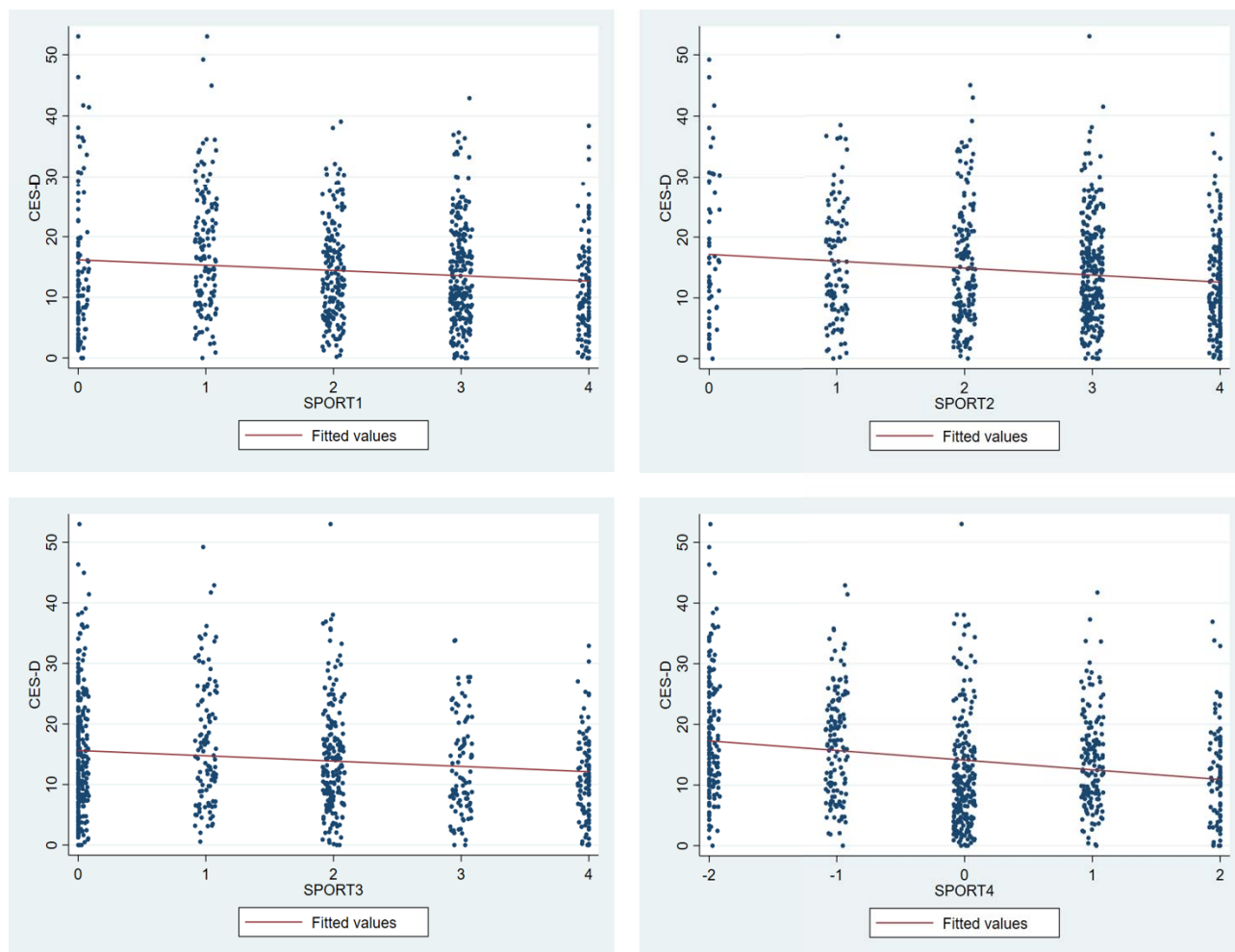

Note: CES-D - Center for Epidemiologic Studies Depression Scale; SLEEP1: "The quality of my sleep has changed recently" - 2=Much worse, -1=A little bit worse, 0=The same, 1=A little better, 2=Much better; SLEEP2: "I tend to stay up late and sleep for many hours during the day" 0=Almost never, 1=Rarely, 2=Sometimes, 3=Often, 4=Almost always; SLEEP3: "I take sleeping pills to help me sleep at night" 0=Almost never, 1=Rarely, 2=Sometimes, 3=Often, 4=Almost always; SLEEP4: "I am having dreams in which I feel trapped, over the last 3 weeks" 0=Almost never, 1=Rarely, 2=Sometimes, 3=Often, 4=Almost always

Figure 1. Association between overall CES-D scores and indicators of changes in the quality and quantity of sleep and disrupted circadian rhythm during the first two waves of the COVID-19 pandemic

Associations between changes in physical activity during the pandemic and depression and its different symptom clusters

Overall, each sport related variable shows a significant association with the severity of depression. An association between an increased role of exercise in the prevention of anxiety and a decrease in overall CES-D score (β=-0.94, q=0.004) as well as a decrease on all individual factors was found (CES-D PA: β=-0.36, q=0.001; CES-D Irr-Soc: β=-0.15, q=0.010; CES-D Dep-Som: β=-0.59, q=0.001). A higher degree of considering exercise to be important during the pandemic was associated with a decrease in the overall CES-D score (β=-1.23, q=0.002) and a decrease in all individual factors (CES-D PA: β=-0.45, q=0.002; CES-D Irr-Soc: β=-0.20, q=0.001; CES-D Dep-Som: β=-0.80,

q=0.001). An increased frequency and intensity of physical workout during the pandemic was associated with a lower overall CES-D score (β=-1.00, q=0.001) and a decrease on lack of positive affects (CES-D PA: β=-0.40,q=0.001) and depressed affect and somatic complaints (CES-D Dep-Som: β =-0.66, q=0.001); while its association with decreased irritability and problems with social relationships was nominally significant but did not survive correction for multiple testing (CES-D Irr-Soc: β=-0.10, q=0.060). A positive change in physical activity related to the pandemic was associated with a decrease in the overall CES-D score (β=-1.75, q=0.001) and a decrease on all three factors (CES-D PA: β =-0.68, q<0.0001; CES-D Irr-Soc: β=-0.20, q<0.0001; CES-D Dep-Som: β=-1,18, q<0.0001) (Figure 2, Table 2).

Note: CES-D - Center for Epidemiologic Studies Depression Scale; SPORT1: "Does exercise help you in the prevention of anxiety?" 0=Not at all, 1=A little bit, 2=Moderately, 3=Much, 4=Very much; SPORT2: "Do you consider that exercise is important during this pandemic?" 0=Not at all, 1=A little bit, 2=Moderately, 3=Much, 4=Very much; SPORT3: "Do you have increased the frequency and intensity of your physical workout during this pandemic and lockdown?" 0=Not at all, 1=A little bit, 2=Moderately, 3=Much, 4=Very much; SPORT4: "How much has your physical activity been affected by this epidemic of COVID-19?" -2=It decreased much, -1=It decreased a little, 0=Neither decreased nor increased,1=It increased a little, 2=It increased much.

Figure 2. Association between the overall CES-D score and importance and changes in frequency and intensity of physical activity and sport habits during the first two waves of the COVID-19 pandemic

Table 2. Association between overall CES-D scores, and its three individual factors and sport habits and its changes during the first two waves of the pandemic

| Sport habits	Beta	Std. Err.	t	p	FDR q	95% CI	
SPORT 1	*CES-D overall*						
Does exercise help you in the prevention of anxiety?	-0.94	0.26	-3.67	<0.0001	0.004*	-1.44	-0.44
	Lack of positive affects (CES-D PA)						
0=Not at all,	-0.36	0.1	-3.46	0.001	0.001*	-0.57	-0.16
1=A little bit,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
2=Moderately,	-0.15	0.05	-2.65	0.008	0.010*	-0.25	-0.04
3=Much,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
4=Very much	-0.59	0.18	-3.21	0.001	0.001*	-0.95	-0.23
SPORT 2	*CES-D overall*						
Do you consider that exercise is important during this pandemic?	-1.23	0.27	-4.48	<0.0001	0.002*	-1.77	-0.69
	Lack of positive affects (CES-D PA)						
0=Not at all,	-0.45	0.11	-4.02	<0.0001	0.002*	-0.67	-0.23
1=A little bit,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
2=Moderately,	-0.2	0.06	-3.37	0.001	0.001*	-0.31	-0.08
3=Much,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
4=Very much	-0.8	0.20	-4.08	<0.0001	0.001*	-1.19	-0.42
SPORT 3	*CES-D overall*						
Do you have increased the frequency and intensity of your physical workout during this pandemic and lockdown?	-1	0.23	-4.27	<0.0001	0.001*	-1.45	-0.54
	Lack of positive affects (CES-D PA)						
0=Not at all,	-0.40	0.090	-4.22	<0.0001	0.001*	-0.59	-0.21
1=A little bit,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
2=Moderately,	-0.10	0.050	-1.97	0.049	0.060	-0.20	0
3=Much,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
4=Very much	-0.66	0.17	-3.94	<0.0001	0.001*	-0.98	-0.33
SPORT 4	*CES-D overall*						
How much has your physical activity been affected by this epidemic of COVID-19?	-1.75	0.25	-6.96	<0.0001	0.001*	-2.25	-1.26
	Lack of positive affects (CES-D PA)						
-2=It decreased much,	-0.68	0.1	-6.58	<0.0001	<0.0001*	-0.88	-0.48
-1=It decreased a little,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
0=Neither decreased nor increased,	-0.20	0.060	-3.68	<0.0001	<0.0001*	-0.31	-0.09
1=It increased a little,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
2=It increased much	-1.18	0.18	-6.53	<0.0001	<0.0001*	-1.53	-0.82

Note: 95% CI - 95% Confidence interval;   CES-D - Center for Epidemiologic Studies Depression Scale;
Dep-Som – depressive affect and somatic complaints;   PA – lack of positive affects;   Irr-Soc – irritability and problems
with social relationships;   * significant results surviving correction for multiple testing (FDR q<0.05)

Associations between diet-specific variables and depression and its different symptom clusters

No significant association was found between CES-D scores and the frequency or amount of food consumption (CES-D OVERALL: q=0.308; CES-D PA: q=0.924; CES-D Irr-Soc: q=0.180; CES-D Dep-Som: q=0.132). A significant association was found between the quality of diet and the overall CES-D score (β=-3.01, q<0.0001) (Figure 3) and all three factors (CES-D PA: β=-1.11, q<0.0001; CES-D Irr-Soc: β=-0.45, q<0.0001; CES-D Dep-Som: β=-2.03, q<0.0001), with a healthier diet associated with lower CES-D scores. No association was found between change in body weight and CES-D scores (CES-D overall q=0.131; CES-D PA q=0.073, CES-D Irr-Soc q=0.745, CES-D Dep-Som p=0.276) (Table 3).

DISCUSSION

The circadian system is critical for maintaining optimal health and well-being, its dysregulation increases susceptibility to many pathological conditions including mental disorders, for example mood disorders. In our study we investigated the association between changes in lifestyle and circadian rhythm-related factors and depression during the first two waves of the COVID-19 pandemic. Factors related to circadian rhythm included changes in sleep, physical activity, and diet-specific questions while depression was assessed by its clinically relevant and etiologically likely distinct symptom clusters including anhedonia and lack of positive affects; irritability and problems with social relationships; and depressed affect and somatic complaints.
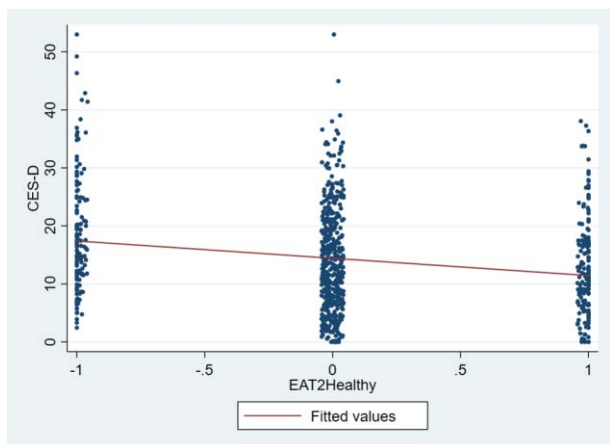
Note: CES-D - Center for Epidemiologic Studies Depression Scale; EAT2Healthy: "Please mark the answer that best represents you during the period of the lockdown" 1=I eat in a healthier way, 0=My eating habits and preferences have not changed, -1=I eat in a more unhealthy way.

Figure 3. Association between the overall CES-D score and the quality of diet during the first two waves of the pandemic

We found significant associations between depression and its three distinct symptom clusters and all factors related to changes in quality and quantity of sleep and diurnal cycle during the pandemic; between depression and its symptom clusters and most factors related to change and importance of physical activity during the pandemic; and change in quality of diet during the pandemic. However, no significant association was found between overall depression or any of its symptom clusters and change in amount of food eaten or change in body-weight during the pandemic. We also did not find differences in the pattern of association in case of depression and its three distinct symptoms clusters: either all or neither of them were associated with a given variable, with the exception of irritability and problems with social relationships, which, unlike the overall depression score and the two other factors, was not associated with change in frequency of physical activity during the pandemic. This indicates a homogenous pattern of association between circadian rhythm-related variables and the different symptom clusters of depression.

Table 3. Associations between the overall CES-D score, the three individual factors and questionnaire items related to one's diet during the first two waves of the pandemic

Diet related questions	Beta	Std. Err.	t	p	FDR q	95% CI	
DIET 1	*CES-D overall*						
During the days of the lockdown did you notice the need to eat larger amounts of food or eat more often?	-0.43	0.41	-1.05	0.294	0.308	-1.24	0.38
	Lack of positive affects (CES-D PA)						
	0.02	0.17	0.1	0.924	0.924	-0.31	0.35
-2=I eat much less than I used to,	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
-1=I eat bit less than I used to,	-0.12	0.09	-1.39	0.164	0.180	-0.30	0.05
0=Neither more nor less,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
1=I eat a bit more than I used to,	-0.46	0.29	-1.57	0.117	0.132	-1.04	0.12
2=I eat much more than I used to							
DIET 2	*CES-D overall*						
Please mark the answer that best represents you during the period of the lockdown	-3.01	0.51	-5.9	<0.0001	<0.0001*	-4.01	-2.01
	Lack of positive affects (CES-D PA)						
	-1.11	0.21	-5.3	<0.0001	<0.0001*	-1.52	-0.7
1=I eat in a healthier way	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
0=My eating habits and preferences have not changed.	-0.45	0.11	-4.09	<0.0001	<0.0001*	-0.67	-0.23
-1=I eat in a more unhealthy way	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
	-2.03	0.37	-5.54	<0.0001	<0.0001*	-2.74	-1.31
DIET 3	*CES-D overall*						
Please mark the answer that best represents you during the period of the lockdown	0.41	0.26	1.59	0.113	0.131	-0.10	0.93
	Lack of positive affects (CES-D PA)						
	0.20	0.11	1.88	0.061	0.073	-0.01	0.41
-2=My body weight has significantly decreased (more than 2-3 kilos),	*Irritability and problems with social relationships (CES-D Irr-Soc)*						
-1=My body weight has slightly decreased (less than 2 kilos lost),	0.02	0.06	0.35	0.728	0.745	-0.09	0.13
0=My body weight is stable,	*Depressed affect and somatic complaints (CES-D Dep-Som)*						
1=My body weight has slightly increased (less than 2 kilos put)	0.21	0.19	1.13	0.257	0.276	-0.15	0.58
2=My body weight has significantly increased (more than 2-3 kilos)							

Note: 95% CI - 95% Confidence interval;   CES-D - Center for Epidemiologic Studies Depression Scale; Dep-Som – depressive affect and somatic complaints;   PA – lack of positive affects;   Irr-Soc – irritability and problems with social relationships;   * significant results surviving correction for multiple testing (FDR q<0.05)

The COVID-19 disease brought about a situation unprecedented in the lives of the majority of the people, and also caused vast changes in their everyday lifestyle, and posed a huge threat not only to our physical health but also our mental wellbeing (Cullen et al. 2020, Gonda & Tarazi 2021). Besides having to adapt to changes encompassing the most basic daily rhythms and physical activity, people had to face huge economic threats directly in their lives and recession in general, and also had to cope with newly emerged problems including isolation and managing their daily lives. Such a situation creates stressful living conditions for the population and may lead to depression via several factors and pathways. Depression in turn leads to less successful adaptation and coping with the new situation, and impaired capacity for self-care and self-sustainment which were already jeopardized by the current pandemic crisis. Thus, understanding the association between lifestyle and circadian changes and depression is crucial for possibly preventing and also treating depression in similar situations, especially considering that lifestyle adjustments and circadian resynchronization have been shown to be effective in treating depression and improving mental well-being and quality of life (Cunningham & Watson 2008, Geoffroy & Palagini 2021, Sarris et al. 2014, Wong et al. 2021). Not surprisingly and in accordance with our expectations, we found markedly significant associations between increased depression and impaired quality of sleep, impaired sleep cycle, necessity of taking sleeping pills and disturbed sleep including nightmares during the pandemic. We also found significant associations between lower depression scores and increased importance of exercise and increased frequency and intensity of physical activity. Similarly, healthier diet was also associated with lower depression scores. It is also notable, that we found no association between depression and amount of food eaten or body weight, thus it seems that quality and not quantity of food is more important in this respect.

One of the major focuses of our study was to investigate the effect of change in circadian rhythm related factors on distinct "subtypes" or symptom clusters of depression during the pandemic. Depression is well-known to be highly heterogeneous (Gonda et al. 2019). It has been reported that in the STAR*D study that there were more than 1000 different depression syndromes observable in at least 5% of patients (Fried & Nesse 2015). Depression is a multifactorial disorder developing based on an interaction between genes and the environment including stress (Gonda et al. 2018), with differing weight of these contributors in case of different subtypes. Thus, it is possible that different depression subtypes or symptom clusters do not only

have divergent neurobiological and genetic backgrounds, but also distinct environmental etiological contributors. Therefore, understanding how different depressive syndromes and symptoms are related to different aspects of environmental stress and consequential lifestyle or circadian rhythm changes would pinpoint specific targets and pathways of prevention.

Furthermore, different subtypes or different symptom clusters of depression respond differently to treatment, for example anhedonia and lack of positive affects are not improved and may even be worsened by selective serotonergic agents (Argyropoulos & Nutt 2013, Price et al. 2009). Besides neurobiological and genetic factors, also environmental factors may contribute to differential treatment response (Kovacs et al. 2014). It is also well known for example that depressed patients exposed to early traumas respond worse to pharmacotherapy in general (Nanni et al. 2012, Xu et al. 2011), and, more importantly, that depressions where the onset of the recent episode was preceded by environmental stress respond worse to SSRI antidepressants in case of carrying certain genetic variants (Keers & Uher 2012, Keers et al. 2011, Mandelli et al. 2009, Xu et al. 2012), highlighting the need for alternative treatment options. Considering the differential relationship between different subtypes or symptomatic clusters of depression and response to treatment, it is especially important to investigate the association between depressive states and lifestyle-related circadian changes during the COVID-19 pandemic, where environmental stress is the major etiological contributor. This may allow to better understand what lifestyle and circadian changes are specifically and separately associated with which symptom cluster, and consequently, bring us closer to a developing differential prevention and intervention possibilities for such situations but also for stress-induced depressive states in general.

Causal inferences cannot be drawn from our data due to the cross-sectional nature of the study, and it is possible that contrary to our hypothesis changes in lifestyle and circadian factors "forced" by the pandemic led to increases in depression, in fact depression triggered by other factors had a negative impact on sleep, physical activity and healthy diet, or that some common underlying factors influenced our variables. Still, the marked positive relationship between the investigated variables suggests that maintaining healthy sleep and circadian rhythms and maintaining or even increasing physical activity may be important protective factors or offer intervention possibilities, also suggesting that psychoeducation concerning this relationship should be considered in similar future situations to prevent deterioration of mental health.

Contribution of individual authors:

Nikolett Beata Vadon, Livia Priyanka Elek, Matyas Szigeti, Berta Erdelyi-Hamza & Xenia Gonda inter-preted the findings.

Nikolett Beata Vadon & Xenia Gonda carried out the background literature search and wrote the first draft of the paper.

Matyas Szigeti carried out the statistical analyses.

Daria Smirnova, Konstantinos N. Fountoulakis & Xenia Gonda conceived the study.

All authors contributed to writing subsequent and final versions of the paper.

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