Decrease in Social Zeitgebers Is Associated With Worsened Delayed Sleep-Wake Phase Disorder: Findings During the Pandemic in Japan

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Decrease in Social Zeitgebers Is Associated With Worsened Delayed Sleep-Wake Phase Disorder: Findings During the Pandemic in Japan

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Background: Delay in sleep-wake rhythms was observed in the general population during the coronavirus disease 2019 (COVID-19) pandemic. Patients with delayed sleep-wake phase disorder (DSWPD) may have also experienced exacerbation of symptoms, but no studies have investigated this topic. In this study, we aimed to retrospectively examine the changes in symptoms of outpatients with DSWPD both before and during the pandemic and to identify the factors associated with the exacerbation of sleep-wake rhythms.

Methods: We included outpatients with DSWPD aged 16 years or older who visited the outpatient clinic due to sleep disorders between January and September 2020. Decreased social zeitgebers was defined as a reduction of 50% or more in the frequency of commuting to school or work during the COVID-19 pandemic. The severity of DSWPD was assessed using the clinical global impressions - severity of illness (CGI-S) at two points: before and during the pandemic. We defined the worsened, unchanged, and improved groups as those whose CGI-S scores worsened by at least one point, remained unchanged, and improved by at least one point, respectively. Multivariate logistic regression analysis was performed to determine the factors associated with worsened DSWPD symptoms.

Results: Sixty patients with DSWPD were eligible for this study. Even before the pandemic, patients who were unemployed or did not attend school tended to show more severe DSWPD symptoms. During the pandemic, 27 patients belonged to the worsened group; 28 patients, unchanged group; and 5 patients, improved group. Decreased social zeitgebers (odds ratio [OR] = 6.668, 95% confidence interval [CI]: 1.653–26.891, $p < 0.05$) and comorbid mood disorders (OR = 8.876, 95% CI: 1.714–45.974, $p < 0.05$) showed independent significant associations with the worsening of DSWPD symptoms.

Conclusions: During the pandemic, the symptoms of DSWPD tended to worsen. The obtained findings emphasize the importance of social zeitgebers, suggesting the need for external motivation in DSWPD treatment.

Keywords: delayed sleep-wake phase disorder, coronavirus disease 2019, COVID-19, state of emergency, Japan, social zeitgeber, bipolar disorder, depression

INTRODUCTION

Circadian rhythm sleep-wake disorders (CRSWDs) are characterized by an inability to synchronize the endogenous circadian rhythm with the daily sleep-wake schedule required for social life, resulting in distress and social disadvantage for the individual (1). CRSWDs consist of several disorders, and delayed sleep-wake phase disorder (DSWPD) is the most common. The prevalence of DSWPD in the general population ranges from 0.1 to 5.1% (2–4), and a higher prevalence (1.1 to 15.9%) has been reported in adolescents and young adults (5–7). DSWPD is known to have serious negative social consequences due to pronounced difficulty falling asleep and waking up at the desired time. These symptoms result in difficulty going to work or school tardiness and absence, as well as falling asleep or poor performance during working hours, with mental health problems, including anxiety and depression (8–11). DSWPD is often comorbid with mood disorders, schizophrenia, and developmental disorders. Moreover, it has been suggested that these comorbidities are associated with worsened symptoms of their own disorders (12–15). DSWPD comorbid with psychiatric or developmental disorders has been reported to have different clinical characteristics compared with primary DSWPD, such as older age, higher rates of unemployment, and poorer treatment responsiveness (10, 16).

Since the intrinsic cycle of the human circadian rhythm is slightly longer than 24 h (17–20), synchronizing factors that advance the circadian phase are considered essential to keep the sleep-wake rhythms synchronized to 24 h. Not only by exposure to high-intensity light immediately after waking (21), non-photic social zeitgebers, such as work and school during the daytime, contribute to preventing delayed sleep-wake phase rhythms (22). However, some people have been in confinement due to the coronavirus disease (COVID-19)-related lockdown, which may have disrupted their sleep-wake rhythms due to the loss of social zeitgebers (23). Delay in bed time and waking time of workers and students as a result of the lockdown has already been reported (24). A tendency toward delayed sleep-wake rhythms during the pandemic has also been indicated in the general population (25–28); thus, the possibility of increased DSWPD development has been pointed out (29).

Patients with DSWPD who are already receiving treatment may also have experienced a delay in their sleep-wake rhythms during the pandemic. Although the vulnerability to circadian rhythm dysregulation in patients with DSWPD has been widely reported (30–32), the association of decreased social zeitgebers during the pandemic with changes in the sleep-wake schedule in patients with DSWPD has not yet been elucidated. Furthermore, no study has investigated how comorbidity with psychiatric or developmental disorders has affected sleep-wake schedules in patients with DSWPD during the COVID-19 pandemic. We hypothesized that worsened DSWPD symptoms would be more pronounced in patients who experienced a significant change in lifestyle, particularly the loss of social zeitgebers due to suspension of commuting to school or work during the pandemic. We also speculated that patients with comorbid psychiatric and developmental disorders would be more likely to experience worsened DSWPD symptoms than those without such disorders, considering their possible vulnerability during the pandemic. We aimed to investigate the changes in the symptoms of DSWPD in outpatients before and during the COVID-19 pandemic to examine the aforementioned hypothesis, as well as to identify the factors associated with the changes in severity among these patients.

METHODS

Participants

We retrospectively reviewed the medical records of patients with DSWPD aged 16 years or older who visited the outpatient clinic of the National Center Hospital of Neurology and Psychiatry for sleep disorders between January and September 2020. Patients with DSWPD who stopped visiting the hospital or had insufficient information were excluded from the analysis. DSWPD diagnosis was confirmed by board-certified sleep medicine physicians of the Japanese Society of Sleep Research (KM, TY, AT, MF, and KK) according to the International Classification of Sleep Disorders, 3rd edition (1).

Measurements

The following demographic and clinical data were retrospectively collected from the medical records: age, sex, body mass index (BMI), school/work status, presence of cohabitants, comorbidity of psychiatric disorders and sleep disorders (except DSWPD), introduction of chronobiological interventions including melatonin agonists (ramelteon and melatonin) and bright light therapy (33), and pharmacological treatment using psychotropic medications other than melatonin agonists. The introduction of chronobiological interventions was investigated at baseline and during the pandemic. However, for psychotropic medications other than melatonin agonists, only the baseline status was assessed due to insufficient information in the medical records. For social zeitgebers, we assessed the frequency of commuting to school and work before and during the COVID-19 pandemic and defined decreased social zeitgeber as a reduction

of 50% or more in the frequency of commuting to school or work under the COVID-19 pandemic than before.

Severity and Change in DSWPD Symptoms

The severity of DSWPD symptoms was retrospectively evaluated using the clinical global impressions - severity of illness (CGI-S) (34) for two periods: baseline, from January to March 2020 (before the COVID-19 pandemic), and endpoint, from April to September 2020 (during the COVID-19 pandemic). CGI-S was scored as follows: 1 = normal, not sick at all; 2 = borderline psychosis; 3 = mild illness; 4 = moderate illness; 5 = marked illness; 6 = severe illness; and 7 = most severe illness. We used the CGI-S because there has been no internationally accepted severity scale for DSWPD. In addition, the CGI-S is simple, can be examined retrospectively using the same criteria, and has been used to rate the severity of DSWPD in some previous studies (35, 36). When determining the CGI-S score, two board-certified psychiatrists of the Japanese Society of Psychiatry and Neurology (RO and KM, KM is also a board-certified sleep medicine physician of the Japanese Society of Sleep Research) evaluated the severity of DSWPD, according to the difference between the desired time and the actual time of sleep onset and awakening and the percentage of days when the patient could fall asleep and wake up at the desired time. In some patients for whom sleep logs and actigraphs were recorded, those results were also accounted. Using the median value of the baseline CGI-S scores, we defined a baseline CGI-S score of 4 or higher as moderate-to-severe DSWPD and a baseline CGI-S score of less than four as mild DSWPD. For the change in symptoms during the pandemic, we used the difference in CGI-S scores between baseline and endpoint: an increase of one or more points as worsened, no change as unchanged, and a decrease of one or more points as improved.

Statistical Analysis

Based on baseline severity, a comparison between mild DSWPD and moderate-to-severe DSWPD was made using the χ^2 test for categorical variables and the Mann–Whitney U-test for the following continuous variables: age, sex, BMI, being a student, presence of cohabitants, comorbidity of psychiatric disorders, comorbidity of sleep disorders other than DSWPD, introduction of chronobiological interventions before the pandemic, and use of psychotropic medications other than melatonin agonists. To investigate the factors associated with worsened DSWPD, logistic regression analysis was conducted for age, sex, BMI, student (yes/no), cohabitation (yes/no), coexistence of psychiatric disorders (schizophrenia/mood disorders/anxiety disorders/intellectual disability, and developmental disorders), coexistence of sleep disorders other than DSWPD (yes/no), and introduction of chronobiological interventions during the COVID-19 pandemic (yes/no). Multiple regression analysis was performed with worsened DSWPD symptoms (i.e., increase of one or more points in CGI-S score) as the dependent variable. All variables were first examined in a univariate model. Then, a multiple regression model was performed on all variables that showed significant correlation in the univariate model to determine the main correlations, controlling for confounding factors. SPSS version 27.0J (SPSS Japan, Inc., Tokyo, Japan) was used for statistical analysis, and the statistical significance level was set at less than 5%.

RESULTS

Of the 108 patients with DSWPD, 48 were excluded because they had interrupted outpatient visits (n = 15), were referred to other outpatient clinics (n = 3), and could not be rated for severity due to insufficient information (n = 30). Finally, 60 patients with DSWPD were included in the analysis. **Table 1** shows the demographic and clinical data of the study subjects. Accordingly, the median age of the total cohort (range) was 24 (16–71) years, and 56.7% of the subjects were male. The median baseline CGI-S score (range) was 3 (2–6), and the median endpoint CGI-S score (range) was 4 (2–6). A total of 26 patients (43.3%) were students, and 20 patients (33.3%) were unemployed or did not attend school at baseline. Notably, 38 patients (63.3%) experienced decreased social zeitgebers during the COVID-19 pandemic. Psychiatric or developmental disorders were comorbid in 26 patients (43.3%): 1 had schizophrenia, 13 had mood disorders (including 9 with major depressive disorder and 4 with bipolar disorder), 6 had anxiety disorders (including 1 with generalized anxiety disorder, 3 with social anxiety disorder, and 2 with obsessive-compulsive disorder), and 11 had developmental disorders (including 2 with attention-deficit/hyperactivity disorder, 8 with autism spectrum disorder, and 1 with both, with some overlap to other psychiatric disorders). The number of patients with sleep disorders other than DSWPD was 18 (30%), including 12 with obstructive sleep apnea, 3 with central hypersomnia (including 2 with narcolepsy type 2, 1 with idiopathic hypersomnia), 3 with sleep-related movement disorders (including 1 with restless legs syndrome and 2 with periodic limb movement disorder), and 1 with parasomnia (sleep-related eating disorder). Forty-four (73.3%) patients received chronobiological interventions and 33 (55%) took psychotropic medications at baseline.

Before the pandemic, 32 and 28 patients were considered to have mild DSWPD and moderate-to-severe DSWPD, respectively, according to the baseline CGI-S score. Comparison between the two groups showed that the moderate-to-severe DSWPD group had significantly more patients who were unemployed or did not attend school (p = 0.001) than the mild DSWPD group. The patients in the mild DSWPD group tended to be older, have a higher BMI, and were more likely to have comorbidities of other sleep disorders than moderate-to-severe DSWPD, but these differences were not significant (p = 0.061, p = 0.064, and p = 0.055, respectively) (**Table 2**).

Baseline and endpoint CGI-S scores showed that 27 patients worsened, 28 remained unchanged, and 5 improved with regard to DSWPD symptoms. For patients with worsened DSWPD symptoms, univariate logistic regression analysis showed that decreased social zeitgebers (odds ratio [OR] = 4.675, 95% confidence interval [CI]: 1.427–15.321, p < 0.05) and comorbidity of mood disorders (OR = 5.882, 95% CI: 1.421–24.355, p < 0.05) were significantly associated. In

TABLE 1 | Demographic and clinical data of patients with DSWPD ($n = 60$).

Age, median (range), year	24.0 (16–71)
Male, *n* (%)	34 (56.7)
BMI, median (range), kg/cm^2	20.5 (15.9–32.3)
Student, *n* (%)	26 (43.3)
Unemployed or did not attend school, *n* (%)	20 (33.3)
Cohabitation, *n* (%)	43 (71.7)
Decreased social zeitgebers, *n* (%)	38 (63.3)
Baseline CGI-S, median (range)[a]	3.0 (2.0–6.0)
Endpoint CGI-S, median (range)[b]	4.0 (2.0–6.0)
Coexisting mental disorders	
Schizophrenia, *n* (%)	1 (1.7)
Mood disorders, *n* (%)[c]	13 (21.7)
Anxiety disorders, *n* (%)[d]	6 (10.0)
Developmental disorders, *n* (%)[e]	11 (18.3)
Other coexisting sleep disorders	
Obstructive sleep apnea, *n* (%)	12 (20.0)
Central disorders of hypersomnolence, *n* (%)[f]	3 (5.0)
Sleep-related movement disorders, *n* (%)[g]	3 (5.0)
Parasomnias, *n* (%)[h]	1 (1.7)
Chronobiological intervention at baseline[i]	44 (73.3)
Psychotropic medications other than ramelteon and melatonin	
Antipsychotics, *n* (%)	15 (25.0)
Antidepressants, *n* (%)	12 (20.0)
Mood stabilizers, *n* (%)	6 (10.0)
Benzodiazepines, *n* (%)	12 (20.0)
Non-benzodiazepines, *n* (%)	7 (11.7)
Orexin receptor antagonists, *n* (%)	8 (13.3)
Psychostimulants, *n* (%)	5 (8.3)

[a] *Baseline CGI-S: before the COVID-19 pandemic.*
[b] *Endpoint CGI-S: during the COVID-19 pandemic.*
[c] *Including major depressive disorder (n = 9) and bipolar disorder (n = 4).*
[d] *Including generalized anxiety disorder (n = 1), social anxiety disorder (n = 3), and obsessive-compulsive disorder (n = 2).*
[e] *Including attention-deficit/hyperactivity disorder (n = 2), autism spectrum disorder (n = 8), and a combination of both (n = 1).*
[f] *Including narcolepsy type two (n = 2) and idiopathic hypersomnia (n = 1).*
[g] *Including restless legs (n = 1) and periodic limb movements (n = 2).*
[h] *Sleep-related eating disorder.*
[i] *Including use of ramelteon or melatonin (n = 37), bright light therapy (n = 1), and combined therapy with both (n = 6).*
DSWPD, delayed sleep-wake phase disorder; BMI, body mass index; CGI-S, clinical global impressions - severity of illness scale.

TABLE 2 | Characteristics of patients before the pandemic: mild vs. moderate-to-severe DSWPD.

	Mild DSWPD ($n = 32$)[a]	Moderate-to-severe DSWPD ($n = 28$)[a]	p[b]
Age, median (range), year	27.5 (16–71)	20.5 (16.0–58.0)	0.061
Male, *n* (%)	19 (59.4)	15 (53.6)	0.651
BMI, median (range), kg/cm^2	21.2 (17.0–32.3)	19.3 (15.9–30.3)	0.064
Student, *n* (%)	11 (34.4)	15 (53.6)	0.134
Unemployed or did not attend school, *n* (%)	6 (18.8)	14 (50.0)	0.010
Cohabitation, *n* (%)	22 (68.8)	21 (75.0)	0.592
Coexisting mental disorders	15 (46.9)	10 (35.7)	0.382
Schizophrenia, *n* (%)	1 (3.1)	0	0.346
Mood disorders, *n* (%)	8 (25.0)	5 (17.9)	0.503
Anxiety disorders, *n* (%)	2 (6.3)	4 (14.3)	0.301
Developmental disorders, *n* (%)	7 (21.9)	4 (14.3)	0.448
Other coexisting sleep disorders	13 (40.6)	5 (17.9)	0.055
Chronobiological intervention at baseline	21 (65.6)	23 (82.1)	0.149
Psychotropic medications other than ramelteon and melatonin	17 (53.1)	16 (57.1)	0.755

[a] *Using the median value of the baseline CGI-S scores, we defined a baseline CGI-S score of four or higher as moderate-to-severe DSWPD and a baseline CGI-S score of less than four as mild.*
[b] *Chi-square test (categorical variables) or Mann-Whitney U-test (continuous variables).*
DSWPD, delayed sleep-wake phase disorder; BMI, body mass index; CGI-S, clinical global impressions - severity of illness scale.

the multiple logistic regression model, both decreased social zeitgebers (OR = 6.668, 95% CI: 1.653–26.891, $p < 0.05$) and comorbidity of mood disorders (OR = 8.876, 95% CI: 1.714–45.974, $p < 0.05$) exhibited independent significant associations (**Table 3**).

During the observation period, only 1 out of the 44 patients discontinued chronobiological interventions. A total of 43 patients received chronobiological interventions during the pandemic: 36 patients received melatonin agonists (melatonin, ramelteon) only, 1 patient received bright light therapy only, and 6 patients received combination therapy of melatonin agonists and bright light therapy. The use of melatonin agonists, bright light therapy, and combinations of these two therapies in these three groups are shown separately in the mild and moderate-to-severe DSWPD groups (**Table 4**). All five patients in the improvement group received chronobiological interventions (four, ramelteon or melatonin only; one, combination therapy with melatonin agonists and bright light therapy). Even under treatment, 14 of the 20 patients in the mild DSWPD group worsened. Meanwhile, the majority of the patients in the moderate-to-severe DSWPD group showed no change in symptoms.

DISCUSSION

The present study examined the changes in severity among patients with DSWPD symptoms during the COVID-19 pandemic. As we hypothesized, reduced social zeitgeber showed an association with worsened severity of DSWPD. Environmental, social, and behavioral factors have already been identified as potentially important in DSWPD treatment (37, 38). However, to the best of our knowledge, this study is the first to address the possible effect of social zeitgebers on symptom severity and course of treatment in DSWPD, even when reviewing the literature prior to the COVID-19 pandemic.

TABLE 3 | Factors associated with worsened DSWPD symptoms[a].

	Univariate relative risk (95% CI)[b]	*p*	Multivariate relative risk (95% CI)[b]	*p*
Age	1.004 (0.965–1.045)	n.s.		
Male sex	0.700 (0.250–1.957)	n.s.		
BMI	1.072 (0.929–1.238)	n.s.		
Student	1.429 (0.511–3.995)	n.s.		
Unemployed or did not attend school	0.388 (0.124–1.212)	n.s.		
Cohabitation	2.514 (0.755–8.368)	n.s.		
Decreased social zeitgebers	4.675 (1.427–15.321)	0.011	6.668 (1.653–26.891)	0.008
Coexisting mental disorders				
Schizophrenia	—	—		
Mood disorders	5.882 (1.421–24.355)	0.015	8.876 (1.714–45.974)	0.009
Anxiety disorders	1.250 (0.231–6.760)	n.s.		
Developmental disorders	0.646 (0.167–2.493)	n.s.		
Other coexisting sleep disorders[c]	0.968 (0.319–2.940)	n.s.		
Chronobiological intervention during the pandemic[d]	1.242 (0.399–3.871)	n.s.		
Psychotropic medications other than ramelteon and melatonin	2.400 (0.837–6.882)	n.s.		

[a]*Using the difference in CGI-S scores before and during the COVID-19 pandemic, we defined the worsened group as one or more points increase.*
[b]*Relative risks approximated to odds ratios.*
[c]*Including obstructive sleep apnea (n = 11), central disorders of hypersomnolence (n = 3), sleep-related movement disorders (n = 2), parasomnias (n = 1), and combination of obstructive sleep apnea with sleep-related movement disorders (n = 1).*
[d]*Including use of ramelteon or melatonin (n = 36), bright light therapy (n = 1), and combination therapy of both (n = 6).*

TABLE 4 | Breakdown of chronobiological intervention during the COVID-19 pandemic, baseline severity of DSWPD, and changes in symptoms.

	Worsened[b] (*n* = 27)	Unchanged[b] (*n* = 28)	Improved[b] (*n* = 5)
Use of ramelteon or melatonin			
Mild[a]	13	5	1
Moderate-to-severe[a]	4	10	3
Bright light therapy			
Mild[a]	1	0	0
Moderate-to-severe[a]	0	0	0
Combination therapy of both			
Mild[a]	0	0	0
Moderate-to-severe[a]	2	3	1
No chronobiological intervention			
Mild[a]	6	6	0
Moderate-to-severe[a]	1	4	0

[a]*Using the median value of the baseline CGI-S scores, we defined a baseline CGI-S score of four or higher as moderate-to-severe DSWPD and a baseline CGI-S score of less than four as mild DSWPD.*
[b]*Using the difference in CGI-S scores before and during the COVID-19 pandemic, we defined the worsened group as one or more points increase, improved group as one or more points decrease, and unchanged group as no change. DSWPD, delayed sleep-wake phase disorder; CGI-S, clinical global impressions - severity of illness scale.*

Although bright light exposure in the morning advances the sleep-wake phase and stabilizes sleep-wake rhythms (21), whether the loss of social zeitgebers resulted in delayed sleep-wake rhythms *via* reduced opportunities for morning light exposure or whether it simply reduced the motivation to wake up in the morning, regardless of light exposure, remains unclear. However, regardless of whether bright light therapy was demonstrated, hospitalization is effective in modulating the sleep-wake rhythms of patients with CRSWD, including DSWPD (39), suggesting the importance of enforcement to wake up in DSWPD treatment. In addition, the moderate-to-severe DSWPD group had more patients who were unemployed or did not attend school than the mild DSWPD group at baseline in the present study. This finding suggests that even before the COVID-19 pandemic, the lack of social zeitgebers may have been associated with the severity of DSWPD or poor response to the intervention. However, poor response to treatment itself might have led to a decrease in social zeitgebers; thus, the causal relationship between the two remains unclear. Recent case reports of DSWPD by Epstein and colleagues indicated that being free from work during the pandemic had delayed sleep rhythms but improved sleep regularity and daytime sleepiness (40). For the two cases presented by them, environmental adjustments that allow the patient to work with a delayed sleep-wake rhythm would be more desirable than enforcing a morning-type sleep-wake rhythm. In the treatment of DSWPD, the main focus has been on advancing the sleep-wake rhythm to meet social needs (33), and the present study suggests that the introduction of factors that motivate or enforce getting up may be effective in this regard. However, given the findings that DSWPD or extreme evening chronotype can be derived from genetic vulnerability (41–44), another goal of treatment, i.e., to improve daily functioning, including employment, while the sleep-wake rhythm remains delayed, can also be an option. Future studies should examine this proposed goal setting in DSWPD treatment, as there is currently no consensus on this

methodology that is not necessarily aimed at modifying the sleep-wake rhythm.

Comorbid mood disorders were significantly associated with worsened DSWPD symptoms independently from decreased social zeitgebers. Comorbidity of DSWPD to mood disorders is common; moreover, it has been suggested that patients with mood disorders are vulnerable to the disruption of sleep-wake schedules (45, 46). During the COVID-19 pandemic, symptoms of depression and anxiety in patients with major depressive disorder and bipolar disorder worsened (47, 48). Particularly for bipolar disorder, CRSWD is considered to be closely related to its pathogenesis (49); lockdown may have led to the recurrence of depressive symptoms in patients with bipolar disorder through the dysregulation of sleep-wake rhythms (50). Considering that psychiatric symptoms, such as anxiety and depression, are known to cause disruptions in sleep-wake rhythms (13), such co-occurrence of exacerbation in mood symptoms and sleep-wake rhythm dysregulations during the pandemic may have occurred not only in patients with bipolar disorder but also in those with mood disorders in general. The subjects in the present study may have also had worsened DSWPD symptoms combined with exacerbation of mood episodes. However, due to the lack of information on changes in the severity of psychiatric symptoms, we could not examine the association between mood episodes and sleep-wake rhythm disorders. To evaluate the relationship between mood symptoms and sleep-wake rhythms, future studies should investigate the severity of mood symptoms as well as changes in sleep-wake rhythms.

Although chronobiological treatments, including bright light therapy and pharmacological treatment with melatonin agonists, have been recognized as effective for sleep-wake dysregulation in patients with DSWPD (51–54), the protective effect of chronobiological interventions on the exacerbation of DSWPD symptoms during the pandemic was not suggested in the present study. In this study, 23 out of the 28 patients in the moderate-to-severe DSWPD group had already received chronobiological interventions before the COVID-19 pandemic. This result suggests that a certain subset of patients with DSWPD does not respond well to the treatments. Moreover, 14 of the 21 patients in the mild DSWPD group who received chronobiological interventions also had worsening of DSWPD symptoms during the pandemic. These results indicate that the maintenance of social synchronization factors may be a prerequisite for the effectiveness of chronobiological interventions. However, of note, all of the five patients who improved during the COVID-19 pandemic (including three patients with decreased social zeitgebers) received chronobiological interventions. Therefore, although its efficacy rate may not be high, the use of melatonin agonists or bright light therapy could still be beneficial in patients with DSWPD. To date, the treatment of DSWPD, particularly interventions for refractory cases, has not been well established (33). Therefore, the development and evaluation of efficacious chronobiological interventions are warranted in future research.

This study had several limitations that should be addressed. First, it was a retrospective study at a single institution that has a specialized outpatient clinic for sleep disorders. Furthermore, only the CGI-S was used to assess severity, and the detailed records of sleep habits were not examined. We also did not use the CGI-I score because we had limited medical record information, and it was difficult to assess the level of improvement in detail on a seven-point scale. In addition, a multinomial logistic analysis using the unchanged group as a reference would have been preferable given that some of the subjects had improved in their DSWPD symptoms. However, we did not employ that analysis in the present study due to the small sample size. Second, changes in sleep-wake rhythms during the lockdown could be explained by several factors, including increased screen exposure time, loss of regularity in dietary rhythms, decreased physical activity, and changes in daytime light exposure (55). In particular, exposure to blue light can delay the sleep onset latency (25, 56); yet, the effect of increased exposure to blue light due to longer screen time during the pandemic (57) was not examined in this study. Future studies should comprehensively investigate the living conditions potentially affecting sleep-wake rhythms. Third, the levels of psychiatric and physical symptoms were not assessed. Furthermore, although various stressors due to the pandemic may have affected sleep-wake rhythms, either directly or through depressive symptoms, these stress factors were not controlled for in this study.

CONCLUSION

The symptoms of DSWPD tended to worsen during the pandemic. The decrease in social zeitgebers following the COVID-19 pandemic was suggested to be a major factor in the exacerbation of symptoms in patients with DSWPD. The importance of social zeitgebers, i.e., external enforcement to waking up, has been emphasized; it may have been linked to stabilizing sleep-wake rhythms more than the treatments that are conventionally considered effective for DSWPD. Hence, the active implementation of social zeitgebers could be a novel intervention in DSWPD treatment. Further studies should clarify the impact of patient characteristics or mood symptoms on therapeutic response and the effectiveness of external enforcement in DSWPD treatment.

DATA AVAILABILITY STATEMENT

The clinical datasets of participants presented in this article are not readily available due to ethical reasons. Requests to access the datasets should be directed to KM, matsui.kentaro@ncnp.go.jp.

ETHICS STATEMENT

This study was approved by the Ethics Committee of the National Center for Neurology and Psychiatry Hospital (A2020-092). Written informed consent from the participants' legal guardian/next of kin was not required to participate in this

study in accordance with the National Legislation and the Institutional Requirements.

AUTHOR CONTRIBUTIONS

RO, KM, TY, KN, TU, AT, NA, MH, MF, and KK contributed to the study design, data collection, result interpretation, and manuscript preparation. RO and KM performed the statistical analysis of the data. RO, KM, and KK drafted the manuscript. All authors contributed to the article and approved the submitted version.

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主論文の要約

氏名：大槻　怜

主論文題名：Decrease in Social Zeitgebers Is Associated With Worsened Delayed Sleep-Wake Phase Disorder: Findings During the Pandemic in Japan

論文題名和訳：社会同調因子の減少は睡眠・覚醒相後退障害の増悪と関連する：日本における COVID-19 流行拡大時の知見

背景

睡眠・覚醒相後退障害（delayed sleep-wake phase disorder：DSWPD）は、生体リズムの遅れにより睡眠時間帯が極端に後退する睡眠障害である。睡眠障害国際分類第 3 版では、望まれる入眠時刻および覚醒時刻に対し、睡眠エピソードが著しく後退しており、そのような状態が 3 ヶ月以上持続している場合に診断される（1）。DSWPD 患者では、学校や仕事の前夜に十分な睡眠時間を確保する上で適当と思われる時間帯に就床しても眠ることができず、深夜から明け方になってようやく入眠する。また、いったん寝付くと正常な時間の睡眠を得るため、登校や出勤のために起床すべき時刻に覚醒することが困難となる。無理に起床した場合も、眠気や集中力低下などにより学業や業務に支障が生じる。DSWPD は青年・若年成人に多く、その有病率は 1.1%～15.9%と考えられている（2-4）。しばしばうつ病や双極性障害（躁うつ病）などの気分障害や発達障害と併存することがあり、このような精神疾患・発達障害併存例においては治療反応性が低下することが報告されている(5)。

ヒトの内因性概日リズムの周期は 24 時間よりも少し長く（6-9）、体内時計中枢は同調因子（zeitgeber）を手がかりに概日リズムを外界の明暗サイクルに同調させている。同調因子として最も重要と考えられているのは、覚醒直後の高照度光への曝露である

が、日中の職場や学校における活動などの社会同調因子も重要と考えられている（10）。

新型コロナウイルス（COVID-19）感染症流行に伴うロックダウンは社会同調因子の減少をもたらし、その結果として就寝時間と起床時間を遅延させたことが一般住民を対象とした調査にて報告されているが（11）、DSWPD患者においてCOVID-19流行に伴う社会生活変化が病状にどのような影響を与えたかについては明らかにされていない。

本研究では、以下の仮説を設定し、検討した。1）流行拡大時に通学・出勤の停止など社会同調因子の減少を経験したDSWPD患者は、そうでない患者に比べて症状が悪化する。2）精神疾患や発達障害を併存するDSWPD患者は、併存疾患のない患者に比べ、流行拡大中に症状が悪化する。

目的

本研究では、COVID-19流行拡大前および流行拡大中のDSWPD外来患者の症状変化を調査し、前述の仮説を検討するとともに、重症度変化に関連する要因を特定することを目的とした。

方法

2020年1月から9月の間に国立精神・神経医療研究センター病院の睡眠障害外来を受診した16歳以上のDSWPD患者を対象に、その後の経過を医療記録に基づき後方視的に検討した。通院が中断された、もしくは情報が不十分な患者は除外した。DSWPDの診断は、睡眠障害国際分類第3版（1）に基づいて、日本睡眠学会認定睡眠認定医によって行われた。医療記録から、流行拡大前および流行拡大中の人口統計学的および臨床データを抽出した。具体的には、年齢、性別、ボディマス指数（BMI）、通学・就労の状況、同居人の有無、精神障害や睡眠障害（DSWPD以外）の併存、メラトニンアゴニスト（ラメルテオンとメラトニン）と高照度光療法を含む時間生物学的介入の有無、およ

びメラトニンアゴニスト以外の向精神薬による薬物療法の有無が調査された。時間生物学的介入は流行拡大前後で評価されたが、メラトニンアゴニスト以外の向精神薬の使用状況については、医療記録の情報が不十分なため、流行拡大前のみについて評価した。社会同調因子の減少を定義した先行研究がないため、COVID-19 の流行拡大前と流行拡大中の通学・通勤の頻度で評価し、COVID-19 流行拡大中の通学・通勤の頻度が流行拡大前よりも 50%以上減少している場合を「社会同調因子の減少」と定義した。流行拡大前に無職・不登校の場合は「減少なし」に分類した。

DSWPD の重症度については確立した評価尺度が存在しないため、複数の先行研究で用いられている CGI-S（clinical global impressions - severity of illness）（12）を使用した。CGI-S は、臨床医が過去に経験した同疾患の患者と比較して、患者の全体的な症状の重症度について 7 段階で疾患の重症度を評価する尺度である。2020 年 1 月から 3 月までのベースライン（COVID-19 流行拡大前）と 2020 年 4 月から 9 月までのエンドポイント（COVID-19 流行拡大中）の 2 期間について、DSWPD の重症度を CGI-S にて後方視的に評価した。DSWPD の診療経験を有する 2 名の医師が協議し、希望する入眠・覚醒時刻と実際の入眠・覚醒時刻の差、および患者が希望する時刻に入眠・起床できた日数の割合に基づき、1 =正常、2 =境界、3 =軽症、4 =中等症、5 =中等症から重症、6 =重症、7 =最重症として点数化した。4 以上を中等症から重症の DSWPD、4 未満を軽症の DSWPD と定義した。流行拡大中の症状変化については、ベースライン時とエンドポイント時の CGI-S スコアの差を用い、1 ポイント以上上昇した場合を「悪化」、変化がない場合を「不変」、1 ポイント以上低下した場合を「改善」と定義した。

統計解析

まず、流行拡大前における軽症群と中等症～重症群の背景情報（年齢、性別、BMI、学籍の有無、無職もしくは不登校、同居者の有無、精神疾患の併存の有無、DSWPD 以外の睡眠障害の併存の有無、流行拡大前の時間生物学的介入の状況、 メラトニンアゴ

ニスト以外の向精神薬の服用の状況）を比較した。カテゴリ変数には χ 二乗検定を用い、連続変数にはMann-Whitney U検定を用いた。

次に、DSWPDの悪化要因はロジスティック回帰分析を用いて検討した。DSWPD症状悪化の有無（CGI-S スコアの 1 ポイント以上の増加）を目的変数とし、年齢、性別、BMI、学籍、無職もしくは不登校、同居者、社会同調因子の減少、精神疾患（統合失調症/気分障害/不安障害）または発達障害の併存、DSWPD 以外の睡眠障害の併存、流行拡大時に時間生物学的介入の有無を説明変数とした。要因解析にあたっては、はじめに単変量モデルにて評価し、次いで、単変量モデルで有意な相関を示した全変数を説明変数とした多変量モデルにて評価した。統計解析には SPSS バージョン 27.0J を用い、統計的有意水準は5%未満とした。

結果

ベースライン期間に受診したDSWPD患者は108人であった。そのうち、外来受診を中断した患者（n = 15）、他の外来診療所に紹介された患者（n = 3）、情報が不十分なために重症度を評価できなかった患者（n = 30）は除外され、60人の患者が解析対象となった。解析対象者の人口統計学的および臨床データを表 1 に示す。38 人の患者（63.3%）が COVID-19 流行拡大中に社会同調因子の減少を経験していた。精神障害または発達障害の併存は26人（43.3%）であった。

表 1. DSWPD患者の人口統計学的および臨床的データ （n = 60）

年齢、中央値（範囲）、歳	24.0 (16-71)
男性、人数（%）	34 (56.7)
BMI、中央値（範囲）、kg/cm^2	20.5 (15.9-32.3)
学生、人数（%）	26 (43.3)
無職もしくは不登校、人数（%）	20 (33.3)
同居者あり、人数（%）	43 (71.7)
社会同調因子の減少あり、人数（%）	38 (63.3)

ベースラインの CGI-S、中央値（範囲）[a]	3.0 (2.0-6.0)
エンドポイントの CGI-S、中央値（範囲）[b]	4.0 (2.0-6.0)
精神疾患の併存	
統合失調症、人数（%）	1 (1.7)
気分障害、人数（%）[c]	13 (21.7)
不安障害、人数（%）[d]	6 (10.0)
発達障害、人数（%）[e]	11 (18.3)
他の睡眠障害の併存	
閉塞性睡眠時無呼吸、人数（%）	12 (20.0)
中枢性過眠症、人数（%）[f]	3 (5.0)
睡眠関連運動障害、人数（%）[g]	3 (5.0)
睡眠時随伴症、人数（%）[h]	1 (1.7)
ベースライン時で時間生物学的介入あり [i]	44 (73.3)
ラメルテオンとメラトニン以外の向精神薬あり	
抗精神病薬、人数（%）	15 (25.0)
抗うつ薬、人数（%）	12 (20.0)
気分安定薬、人数（%）	6 (10.0)
ベンゾジアゼピン系、人数（%）	12 (20.0)
非ベンゾジアゼピン系、人数（%）	7 (11.7)
オレキシン受容体拮抗薬、人数（%）	8 (13.3)
精神刺激薬、人数（%）	5 (8.3)

[a] ベースラインの CGI-S：COVID-19 流行拡大前。

[b] エンドポイントの CGI-S：COVID-19 流行拡大中。

[c] 大うつ病性障害 (n = 9)、双極性感情障害 (n = 4) を含む。

[d] 全般性不安障害 (n = 1)、社交不安障害 (n = 3)、強迫性障害 (n = 2) を含む。

[e] 注意欠陥多動性障害 (n = 2)、自閉症スペクトラム障害 (n = 8)、両疾患の併存 (n = 1) を含む。

[f] ナルコレプシー type 2 (n = 2)、特発性過眠症 (n = 1) を含む。

[g] むずむず脚症候群 (n = 1)、周期性四肢運動障害 (n = 2) を含む。

[h] 睡眠関連摂食障害。

[i] ラメルテオンもしくはメラトニン (n = 37)、高照度光療法 (n = 1)、両治療の併用 (n = 6) を含む。

DSWPD, delayed sleep-wake phase disorder ; BMI, body mass index ; CGI-S, clinical global impressions - severity of illness scale。

流行拡大前の CGI-S スコアから、32 名と 28 名の患者が、それぞれ軽症の DSWPD、中

等症～重症の DSWPD と分類された（表 2）。2 群間の比較では、軽症群よりも中等症～重症群で無職もしくは不登校の患者が多かった（p = 0.001）。軽症群は、中等症～重症群よりも高齢で、BMI が高く、DSWPD 以外の睡眠障害の併存を有する傾向があったが、これらの差は有意ではなかった（それぞれ p = 0.061、p = 0.064、p = 0.055）。

表 2. 流行拡大前の患者の特徴：軽症と中等症から重症の DSWPD の比較

	軽症（n = 32）[a]	中等症から重症（n = 28）[a]	p [b]
年齢、中央値（範囲）、歳	27.5 (16-71)	20.5 (16.0-58.0)	0.061
男性、人数（%）	19 (59.4)	15 (53.6)	0.651
BMI、中央値（範囲）、kg/cm^2	21.2 (17.0-32.3)	19.3 (15.9-30.3)	0.064
学生、人数（%）	11 (34.4)	15 (53.6)	0.134
無職もしくは不登校、人数（%）	6 (18.8)	14 (50.0)	0.010
同居者あり、人数（%）	22 (68.8)	21 (75.0)	0.592
精神疾患の併存あり	15 (46.9)	10 (35.7)	0.382
統合失調症、人数（%）	1 (3.1)	0	0.346
気分障害、人数（%）	8 (25.0)	5 (17.9)	0.503
不安障害、人数（%）	2 (6.3)	4 (14.3)	0.301
発達障害、人数（%）	7 (21.9)	4 (14.3)	0.448
他の睡眠障害の併存あり	13 (40.6)	5 (17.9)	0.055
流行拡大前に時間生物学的介入あり	21 (65.6)	23 (82.1)	0.149
ラメルテオンとメラトニン以外の向精神薬あり	17 (53.1)	16 (57.1)	0.755

[a] ベースラインの CGI-S スコアの中央値を用いて、ベースラインの CGI-S スコアが 4 以上を中等症から重症の DSWPD、4 未満を軽症と定義した。

[b] χ 二乗検定（カテゴリー変数）または Mann-Whitney U 検定（連続変数）。

流行拡大前と流行拡大中の重症度変化については、27 人が悪化、28 人が不変、5 人が改善した。悪化した患者について単変量ロジスティック回帰分析を行った結果、社会同調因子の減少（オッズ比[OR] = 4.675、95%信頼区間[CI]：1.427-15.321、p < 0.05）と気分障害の併存（OR = 5.882、95%CI：1.421-24.355、p < 0.05）　が有意に関連してい

た。多変量ロジスティック回帰モデルでは、社会同調因子の減少（OR = 6.668、95%CI：1.653-26.891、$p < 0.05$）と気分障害の併存（OR = 8.876、95%CI：1.714-45.974、$p < 0.05$）が独立して症状悪化に有意な関連を示した（表3）。Hosmer-Lemeshowの適合度は$p = 0.959$であり、モデルの適合度は良好であった。また、すべての変数で分散拡大係数(VIF)が10未満であり多重共線性はなかった。

表 3. **DSWPD**症状の悪化に関連する因子 [a)]

	単変量相対危険度 (95% CI) [b)]	p	多変量相対危険度 (95% CI) [b)]	p
年齢	1.004 (0.965-1.045)	**n.s.**		
男性	0.700 (0.250-1.957)	**n.s.**		
BMI	1.072 (0.929-1.238)	**n.s.**		
学生	1.429 (0.511-3.995)	**n.s.**		
無職もしくは不登校	0.388 (0.124-1.212)	**n.s.**		
同居者あり	2.514 (0.755-8.368)	**n.s.**		
社会同調因子の減少あり	4.675 (1.427-15.321)	0.011	6.668 (1.653-26.891)	0.008
精神疾患の併存あり				
統合失調症	–	–		
気分障害	5.882 (1.421-24.355)	0.015	8.876 (1.714-45.974)	0.009
不安障害	1.250 (0.231-6.760)	**n.s.**		
発達障害	0.646 (0.167-2.493)	**n.s.**		
他の睡眠障害の併存あり [c)]	0.968 (0.319-2.940)	**n.s.**		
流行拡大中に時間生物学的介入あり [d)]	1.242 (0.399-3.871)	**n.s.**		
ラメルテオンとメラトニン以外の向精神薬あり	2.400 (0.837-6.882)	**n.s.**		

[a)] **COVID-19**流行拡大前後の**CGI-S**の点数を用いて、1ポイント以上点数の差が上昇した場合を悪化と定義した。

[b] 相対リスクはオッズ比に近似。

[c] 閉塞性睡眠時無呼吸（n=11）、中枢性過眠症　（n=3）、睡眠関連運動障害（n=2）、睡眠時随伴症（n=1）、閉塞性睡眠時無呼吸と睡眠関連運動障害の合併（n=1）を含む。
[d] ラメルテオンもしくはメラトニン　（n=36）、高照度光療法　（n=1）、両治療の併用　（n=6）。

時間生物学的介入が行われていた 44 人の患者のうち 1 人が観察期間中に介入を中止されており、流行拡大中においては 43 人が時間生物学的介入を受けていた。そのうち、36 人はメラトニンアゴニスト（メラトニン、ラメルテオン）の投与のみを受け、1 人は高照度光療法のみを受け、6 人はメラトニンアゴニストの投与と高照度光療法の両方を受けていた。重症度変化（悪化、不変、改善）別の治療内容内訳を表 4 に示す。

改善群の全患者（n = 5）が時間生物学的介入を受けていた（4 人はラメルテオンまたはメラトニンのみ、1 人はメラトニンアゴニストと高照度光療法の両方）。ベースライン時に軽症であった全患者（n = 20）がいずれかの時間生物学的介入を受けていたが、14 人が悪化した。一方、ベースライン時における中等症～重症群の大部分は症状の変化を示さなかった。

表 4. COVID-19 流行拡大中の時間生物学的介入の内訳、DSWPD の流行拡大前の重症度からの症状変化.

	増悪 [b] (n = 27)	変化なし [b] (n = 28)	改善 [b] (n = 5)
ラメルテオンもしくはメラトニン服用			
軽症 [a]	13	5	1
中等症から重症 [a]	4	10	3
高照度光療法			
軽症 [a]	1	0	0
中等症から重症 [a]	0	0	0
両治療の併用			
軽症 [a]	0	0	0

中等症から重症 [a]	2	3	1
時間生物学的介入なし			
軽症 [a]	6	6	0
中等症から重症 [a]	1	4	0

[a] 流行拡大前の CGI-S スコアの中央値を用いて、4 点以上を中等症から重症の DSWPD、4 点未満を軽症と定義した。
[b] COVID-19 流行前と流行中の CGI-S スコアの差を用いて、1 点以上上昇した場合を悪化群、1 点以上低下した場合を改善群、変化なしを変化群と定義した。

DSWPD、delayed sleep-wake phase disorder；CGI-S、clinical global impressions - severity of illness scale。

考察

COVID-19 流行拡大に伴う社会同調因子の減少は DSWPD 症状の悪化と関連していた。健常者においては社会同調因子の低下が概日リズムを後退させることが報告されている（13）。このことから、DSWPD においても社会同調因子の減少が病状の悪化を招く可能性が推測されていたが、これまで明確なエビデンスはなかった。本研究は、多くの個人において登校・出勤が制限されるという社会変化をもたらした COVID-19 の流行拡大に着目し、社会同調因子の減少が DSWPD の悪化要因になることを示した初めての研究である。

社会同調因子の減少、すなわち通学・通勤頻度の減少は、日中の高照度光への曝露の機会を減少させ、その結果として症状の悪化を招いた可能性がある。しかし、日中の高照度光への曝露の有無に関わらず、入院治療が睡眠・覚醒リズムの適正化に有効であったという先行研究の結果を踏まえると（14）、高照度光への曝露のみならず、起床の動機自体が重要である可能性がある。

DSWPD 治療では、生活指導や時間生物学的介入によって後退した睡眠・覚醒リズムを前進させるが（15）、本研究の結果は、その際に社会同調因子を積極的に導入することも有効である可能性を示唆する。しかし一方で、COVID-19 流行に伴うロックダウン下で、後退した睡眠・覚醒リズムに合わせ就労スケジュールを変更したことにより症状

が安定し、服用薬を減量できたという症例報告がある（16)。したがって、感染症流行等により外出が制限される特殊な状況においては、在宅で睡眠相前進を目的とした従来の DSWPD 治療を継続するよりも、就労スケジュールの変更を検討する方が合理的かもしれず、この点についてはさらなる知見の集積が望まれる。

併存する気分障害は、社会同調因子の減少とは独立して DSWPD 症状の増悪に関連していた。気分障害にはうつ病や双極性障害（躁うつ病）が含まれ、抑うつ病相のみを示す場合はうつ病、抑うつ状態と躁状態の両病相を示す場合は双極性障害と診断される。これらの気分障害患者は、睡眠・覚醒リズムが不安定になりやすく DSWPD を合併しやすい（17、18)。また、不安や抑うつなどの精神症状は睡眠・覚醒リズムの乱れを引き起こすことが報告されている（19)。COVID-19 の流行拡大中に気分障害患者の抑うつや不安が悪化することが知られており（20、21)、本研究に参加した気分障害併存 DSWPD 患者も気分症状の悪化により DSWPD 症状が増悪した可能性がある。しかし、本研究では精神症状に関する情報を十分に調査しておらず、その関連性については検討できなかった。

一般的に、高照度光療法やメラトニンアゴニストによる時間生物学的介入は、DSWPD 患者に有効であると認識されている（22-25)。しかし、流行拡大前において時間生物学的介入を受けていたにもかかわらず中等症～重症の患者がいた。また、流行拡大前は軽症であり時間生物学的介入を継続したにも関わらず流行拡大中に中等症～重症に移行した患者もおり、時間生物学的介入の効果は一部の患者においては限定的であると考えられる。流行拡大前の中等症～重症群には無職ないし不登校の患者の割合が多かったこと、社会同調因子の減少が流行拡大中の症状悪化に関連していたという今回の結果を踏まえると、時間生物学的介入が奏功するためには、社会同調因子の維持が前提となる可能性がある。

本研究には、いくつかの限界が存在する。まず、難治例や精神疾患を合併した症例が集まりやすい医療機関を受診した患者を対象とした単一施設における研究であり、結果

の一般化には限界がある。また、後ろ向き研究であり、医療記録情報も限定されていた。重症度は CGI-S で評価しており、重症度に関連し得る詳細な睡眠習慣や昼間の生活の質、本人の日常生活の満足度、精神状態は評価できていない。さらに、改善度を詳細に評価することが困難であったため、CGI-I（clinical global impressions - improvement）（12）は用いず、重症度変化を CGI-S の差で評価している。CGI-S については、標準化されたスコアリングガイドラインに従って評価したが、臨床医の経験に基づいているため、測定誤差が生じる可能性が否定出来ない。さらに、一部の患者ではパンデミック下で DSWPD 症状が改善したことを考えると、変化のなかった群を対照とした多項ロジスティック解析にて悪化および改善の関連要因を評価することが望ましいが、患者数が少なく採用しなかった。今後、改善群に着目した研究を実施することが必要である。次に、本研究では通勤・通学の頻度を社会同調因子と定義している。しかしこれ以外にも、パンデミック下においては、家族や友人との接触機会や、アルバイトや習い事などのための外出機会も減少したと考えられるが、これらの社会同調因子の影響は検討していない。また、流行拡大中の睡眠・覚醒のリズムの変化は、電子画面を見る時間の増加、食事リズムの規則性の喪失、身体活動の低下、日中の光曝露の減少などの要因によって説明できる（26）。特に、電子画面を見る時間の増加は入眠潜時を遅延させる青色光への曝露につながるが、この研究では評価・検討されなかった。今後の研究では、睡眠・覚醒のリズムに影響を与える可能性のある要因について包括的に調査する必要がある。さらに、日本では、長引くパンデミック中に不定期に外出自粛を求める措置が発出されたため、時期によって外出頻度は変化したと予想される。そのため、調査時期により重症度が変化した可能性があるが、この点の評価は行えていない。今後、重症度変化の推移に関する縦断的検討が望まれる。最後に、精神および身体症状の程度は評価されなかった。様々なストレス要因が、直接的または間接的に睡眠・覚醒リズムに影響を与えた可能性があるが、これらのストレス要因はこの研究では制御されていない。

まとめ

DSWPDの症状は、COVID-19流行拡大中に社会同調因子の減少を経験した患者で増悪する傾向があり、DSWPD患者の症状悪化の主要要因であることが示唆された。本研究の結果は、DSWPD治療における社会同調因子の重要性を示唆しており、社会同調因子の積極的な導入により改善率を高められる可能性がある。今後、DSWPD治療における社会同調因子の維持、すなわち就労や就学など起床の動機付けを積極的に行うことの有効性を明らかにすることが望まれる。

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