

# Changes in Sleep Pattern During the COVID-19 Lockdown in Patients With Narcolepsy, Idiopathic Hypersomnia, and Restless Legs Syndrome

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## Abstract

### Background and Objectives

To explore the first coronavirus disease 2019 (COVID-19) lockdown effect on sleep symptoms in patients with narcolepsy, idiopathic hypersomnia (IH), and restless legs syndrome (RLS).

### Methods

Between March and May 2020, a sample of adult patients regularly followed up in a Reference Hospital Sleep Unit (299 with narcolepsy, 260 with IH, and 254 with RLS) was offered an online survey assessing their sleep-wake habits, daily activities, medication intake, and validated scales: International RLS Study Group questionnaire, Narcolepsy Severity Scale (NSS), IH Severity Scale (IHSS), Epworth Sleepiness Scale (ESS), Insomnia Severity Index, Beck Depression Inventory–II, and European Quality of Life (QoL) scale. The survey was proposed once, and the questions were answered for the prelockdown (recall of the month before the confinement) and the lockdown (time of study) periods.

### Results

Overall, 331 patients completed the survey (response rate 40.7%): 102 with narcolepsy, 81 with IH, and 148 with RLS. All patients reported later bedtimes, with reduced differences for time in bed (TIB) and total sleep time (TST) over 24 hours between weekdays and weekends. Patients with narcolepsy spent more TIB and increased TST overnight, with more daytime napping. They had more awakenings, higher ESS scores, lower QoL, and no NSS changes. Patients with IH also increased their TIB, TST overnight and 24 hours on weekdays. Nocturnal sleep latency and the number of awakenings increased but with no change in ESS, QoL, and IHSS scores. Patients with RLS reported longer nocturnal sleep latency, more awakenings, more naps, decreased TIB, and TST overnight. RLS severity increased while QoL decreased. A significant portion of patients reported disease worsening during the lockdown (narcolepsy: 39.4%, IH: 43.6%, and RLS: 32.8%), and some patients stopped or lowered their medication (narcolepsy: 22.5%, IH: 28%, and RLS: 9.5%).

### Discussion

During the lockdown, all patients reported later bedtimes; those with narcolepsy and IH extended their sleep duration unlike patients with RLS. These changes were often associated with negative consequences on QoL. In the current context of recurrent COVID-19 waves, the recent development of teleconsultations should enable physicians to monitor patients with chronic sleep disorders more closely and to recommend optimized sleep schedules and duration, in order to prevent psychological problems and improve their QoL.

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## Glossary

**BDI-II** = Beck Depression Inventory–II; **COVID-19** = coronavirus disease 2019; **DNS** = disrupted nocturnal sleep; **EQ-5D** = European QoL 5-dimensions; **ESS** = Epworth Sleepiness Scale; **ICSD-3** = Third International Classification of Sleep Disorders; **IH** = idiopathic hypersomnia; **IHSS** = IH Severity Scale; **IRLS** = International RLS Study Group questionnaire; **ISI** = Insomnia Severity Index; **MSLT** = Multiple Sleep Latency Test; **NSS** = Narcolepsy Severity Scale; **NT1** = narcolepsy type 1; **NT2** = narcolepsy type 2; **QoL** = quality of life; **RLS** = restless legs syndrome; **TST** = total sleep time; **VAS** = visual analog scale.

The forced social and work distancing during the coronavirus disease 2019 (COVID-19) pandemic lockdown led to several health-related problems such as mood, psychological disturbances, and sleep troubles in the general population.<sup>1-3</sup> Whether this exceptional situation had a similar effect on patients with sleep disorders remains unclear and controversial.<sup>4-7</sup> In March 2020 in France, a nationwide home confinement was established to prevent the spread of COVID-19 infection, and health resources were reallocated, prioritizing the response to COVID-19 during several weeks. Access to routine care was thus restricted or even impossible for patients with chronic disorders.

Narcolepsy type 1 (NT1) and type 2 (NT2) and idiopathic hypersomnia (IH) are rare and disabling central disorders of hypersomnolence affecting mostly young adults.<sup>8</sup> In narcolepsy, excessive daytime sleepiness is severe, and nocturnal sleep has usually a normal duration but is fragmented.<sup>9</sup> In contrast, IH is characterized by prolonged undisturbed nocturnal sleep with long unrefreshing naps and often sleep inertia.<sup>10</sup> Restless legs syndrome (RLS) is a frequent sensorimotor disorder characterized by an urge to move the legs at night, often associated with sleep deprivation and sleep fragmentation, but with infrequent naps or mild excessive daytime sleepiness.<sup>11</sup> Management of these disorders requires, first, a nonpharmacologic approach with good sleep hygiene recommendations and medication for moderate to severe cases.<sup>12-14</sup>

The extended period of home confinement due to COVID-19 could have allowed these patients with different sleep phenotypes, ranging from insomnia to hypersomnia, to adjust their sleep schedules and change their habits. Although home confinement may have resulted in less time constraints for work and daily life, the stressful conditions worsened with reduced opportunities for leisure and outings and less social synchronizers. A few studies reported the effect of quarantine in patients with narcolepsy, but with discrepancies, showing either improvement or worsening of the symptoms,<sup>15-18</sup> and one included patients with IH.<sup>18</sup> Moreover, weekday and weekend sleep habits before the lockdown were not assessed, and no validated measurement tools of disease severity and quality of life (QoL) were available. No data have been published in patients with RLS during the lockdown.

This unique extreme situation that lasted 3 months in France provided an opportunity to assess the evolution of symptoms

of patients with chronic neurologic sleep disorders and their behavioral adjustments in similar and constrained environmental conditions. The aims of the present study were to evaluate with a standardized questionnaire the lockdown effect (1) on sleep, sleep habits, and QoL in 3 samples of patients with a diagnosis of narcolepsy, IH, and RLS and (2) on the disease symptoms and medication intake in each group.

## Methods

### Study Population

Between March 17 and May 11, 2020, in France, the government established the first national lockdown, with a restriction of mobility up to in-home confinement, limiting the movements of the population except for necessity, work, emergencies, and severe health circumstances. Outings were authorized only 1 hour per day in a limited area around the residence. Hospitalizations and consultations of 813 adult patients with narcolepsy, IH, or RLS were canceled during this period in the Sleep Disorder Unit and the National Reference Center for Narcolepsy and Rare Hypersomnias of Montpellier University Hospital, France. These patients regularly followed up in the Sleep Unit (273 with NT1, 26 with NT2, 260 with IH, and 254 with RLS) were contacted by phone or email and were offered an online survey to record the effect of lockdown on their sleep habits and symptoms severity. These exchanges also guaranteed care continuity. All patients who agreed to participate and completed the online survey were included, regardless of medication status, disease severity, or occupation, except shift workers, who were not included.

### Standard Protocol Approvals, Registrations, and Patient Consents

This project was approved by the local ethics committees (Institutional Review Board, Montpellier University Hospital, France). All patients provided consent for use of their answers in this publication. This study is ancillary to the SOMNOBANK project (Constitution of a Clinical, Neurophysiological and Biological Cohort for Chronic Sleep Disorders Responsible of Hypersomnolence, NCT03998020).

### Online Survey

The survey was created by the physicians of Sleep Unit, Montpellier, France, and was composed of questions related to occupations, sleep habits, sleep disorders, and medication intake, with several validated and dedicated scales for sleep symptoms and the 3 different diseases. The survey was

proposed once to the patients, and the questions were answered for the prelockdown (recall of the month before the confinement) and the lockdown (time of study) periods. Daily activities or current working status were recorded and categorized as (1) regular working schedule; (2) working/studying at home; (3) sick leave; (4) partial unemployment or child care; and (5) unemployed or retired. Sleep-wake habits were assessed during weekdays and weekends independently, for the periods just before and during the lockdown: bedtime, wake-up time, time spent in bed and estimated TST overnight and over 24 hours, sleep onset latency, number of awakenings, and presence of daytime napping. Through a Patient Global Opinion scale about their sleep disease, all patients were asked whether the lockdown situation had a direct effect on their sleep disease (no perceived effect/improvement/worsening). Current medication for narcolepsy, IH, and RLS was recorded. All patients were asked to report whether they modified their treatments: stopped, lowered, or increased doses.

Excessive daytime sleepiness before and during the lockdown was evaluated with the Epworth Sleepiness Scale (ESS).<sup>19</sup> QoL before and during the lockdown was assessed with the European QoL 5-dimensions (EQ-5D) visual analog scale (VAS) scores, with higher scores indicating better QoL.<sup>20</sup> The presence and severity of depressive symptoms during the last 2 weeks before the lockdown were evaluated with the Beck Depression Inventory–II (BDI-II).<sup>21</sup> To assess the severity of their symptoms before and during the lockdown, patients with narcolepsy completed the Narcolepsy Severity Scale (NSS)<sup>22,23</sup> (with 1 item on disrupted nocturnal sleep [DNS] complaint and 3 items on partial and generalized cataplexy frequencies and their consequences, further analyzed independently), patients with IH completed the IH Severity Scale (IHSS),<sup>24</sup> and patients with RLS completed the International RLS Study Group questionnaire (IRLS)<sup>25</sup> and the Insomnia Severity Index (ISI)<sup>26</sup> to assess related insomnia symptoms. The complete survey in its original French language is available in the eAppendix ([links.lww.com/WNL/C222](https://links.lww.com/WNL/C222)).

## Statistical Analyses

Demographic and clinical characteristics were described using means and SDs for continuous variables or number and percentages for categorical variables. Comparisons between 2 evaluations (before and during the lockdown) were performed using the Wilcoxon signed-rank test for continuous variables and the Mc Nemar test or Bowker test of symmetry for qualitative variables. For all comparisons, significance was set at  $p < 0.05$ . Statistical analyses were performed using SAS version 9.4.

## Data Availability

The data that support this study's findings are available from the corresponding authors on reasonable request.

## Results

### Participants' Characteristics

Overall, 331 patients were included (response rate 40.71%; 64.65% women, mean age  $48.60 \pm 19.24$  years): 102 with

narcolepsy (88 NT1 and 14 NT2), 81 with IH, and 148 with RLS. In the 102 patients with narcolepsy (60.78% women), the mean age was  $40.11 \pm 19.54$  years. Diagnosis of NT1 and NT2 was previously confirmed based on the Third International Classification of Sleep Disorders (ICSD-3) criteria<sup>27</sup> with a baseline mean sleep latency on the Multiple Sleep Latency Test (MSLT) at  $5.26 \pm 3.65$  minutes, with  $3.46 \pm 1.21$  sleep-onset REM periods. Human leukocyte antigen genotyping was available for 94 patients (81 NT1 and 13 NT2), all NT1 and 9 NT2 carried the allele *DQB1\*06:02*. CSF orexin-A levels were measured for 74 NT1 (mean levels  $27.42 \pm 25.76$  pg/mL, all  $<110$  pg/mL) and 11 NT2 (mean levels  $259.27 \pm 79.95$  pg/mL; 8 patients  $>200$  pg/mL and 3 with intermediate levels).

In the 81 patients with IH (83.95% women), the mean age was  $35.28 \pm 12.83$  years. Diagnosis of IH was previously confirmed based on the ICSD-3,<sup>27</sup> with a baseline MSLT mean sleep latency at  $8.85 \pm 3.61$  minutes, and a prolonged bed-rest PSG recording over a 32-hour period<sup>28</sup> performed in 72 patients, showing a prolonged total sleep time (TST) ( $>19$  hours/32 hours) in 61 (84.72%). CSF orexin-A levels were measured for 25 patients with IH (mean levels  $310.66 \pm 128.36$  pg/mL, all  $>200$  pg/mL, except 2 with intermediate levels).

In the 148 patients with RLS, the mean age was  $61.73 \pm 12.56$  years (56.76% women) and the mean age at RLS onset was  $41.21 \pm 16.45$  years. All patients had the 5 diagnosis criteria based on the International RLS Study Group criteria<sup>11</sup> and ICSD-3,<sup>27</sup> confirmed by medical interview by sleep experts. The mean ferritin levels for 126 patients with available blood sampling were  $184.95 \pm 149.31$   $\mu$ g/L. A PSG recording at baseline was performed in 134 patients in a drug-free condition (mean age  $57.16 \pm 11.57$  years at that time, mean IRLS questionnaire severity scores  $24.67 \pm 6.90$ ) and showed a mean TST at  $326.81 \pm 89.79$  minutes and a mean periodic leg movement index during sleep at  $45.79 \pm 51.42$ /h (67.16% above 15/h).

### Sleep Patterns in Narcolepsy

During the lockdown, 13 (13.83%) patients with narcolepsy had a regular working schedule, 27 (28.72%) were working/studying at home, 7 (7.45%) off work, 16 (17.02%) partially unemployed/child caring, and 31 (32.98%) retired/unemployed. Patients reported an increase in time spent in bed and TST overnight and over 24 hours with more frequent naps on weekdays during the lockdown compared with prelockdown, without significant changes for the weekend period (Table 1). In both weekend and weekdays, the number of awakenings increased during the lockdown period. Patients reported later bedtimes during both weekdays and weekends and later wake-up times only on weekdays. The differences between weekdays/weekends of bedtime, wake-up time, time spent in bed, TST overnight, and TST over 24 hours highly decreased during the lockdown (Table 1). Compared with prelockdown, ESS total scores were higher during the lockdown, with lower QoL scores, without significant changes for the NSS, except for an increase in DNS (43.01% vs 35.48% with moderate/severe DNS,  $p = 0.03$ ). The frequency of

**Table 1** Comparison of Sleep Habits and Self-Questionnaires Before and During the Lockdown in Patients With Narcolepsy

|   | Patients with narcolepsy (N = 102) |                   | p Value              |
|---|------------------------------------|-------------------|----------------------|
|   | Before lockdown                    | During lockdown   |                      |
| <b>Sleep habits: weekdays</b>             |                                    |                   |                      |
| Bed time, h:min                           | 22:48 (0:55)                       | 23:23 (1:12)      | <0.0001 <sup>a</sup> |
| Wake-up time, h:min                       | 07:04 (1:05)                       | 07:59 (1:36)      | <0.0001 <sup>a</sup> |
| Time spent in bed, h:min                  | 8:17 (1:12)                        | 8:37 (1:26)       | 0.01 <sup>a</sup>    |
| Estimated TST at night, h:min             | 7:28 (1:32)                        | 7:47 (1:47)       | 0.01 <sup>a</sup>    |
| Night sleep latency, min                  | 8.51 (7.50)                        | 9.36 (10.23)      | 0.33                 |
| No. of awakenings per night               | 2.20 (1.89)                        | 2.47 (1.19)       | 0.03 <sup>a</sup>    |
| Presence of daytime napping, yes, n (%)   | 74 (79.57)                         | 82 (88.17)        | 0.02 <sup>a</sup>    |
| TST over 24 h, h:min                      | 7:53 (1:31)                        | 8:23 (1:49)       | 0.001 <sup>a</sup>   |
| <b>Sleep habits: weekends</b>             |                                    |                   |                      |
| Bed time, h:min                           | 23:25 (0:59)                       | 23:40 (1:12)      | 0.02 <sup>a</sup>    |
| Wake-up time, h:min                       | 08:26 (1:31)                       | 08:31 (1:35)      | 0.25                 |
| Time spent in bed, h:min                  | 9:03 (1:22)                        | 8:53 (1:25)       | 0.10                 |
| Estimated TST at night, h:min             | 8:07 (1:54)                        | 8:00 (1:54)       | 0.37                 |
| Night sleep latency, min                  | 9.08 (10.19)                       | 9.33 (10.51)      | 0.86                 |
| No. of awakenings per night               | 2.05 (1.83)                        | 2.68 (3.61)       | 0.0003 <sup>a</sup>  |
| Presence of daytime napping, yes, n (%)   | 79 (84.95%)                        | 82 (88.17%)       | 0.26                 |
| TST over 24 h, h:min                      | 8:40:42 (1:59:23)                  | 8:38:57 (1:57:48) | 0.98                 |
| <b>Sleep habits: weekdays vs weekends</b> |                                    |                   |                      |
| DELTA DIFF bedtime, min                   | 37.17 (52.68)                      | 16.25 (30.52)     | <0.0001 <sup>a</sup> |
| DELTA DIFF wake-up time, min              | 82.31 (91.03)                      | 31.88 (53.97)     | <0.0001 <sup>a</sup> |
| DELTA DIFF time spent in bed, min         | 46.03 (72.73)                      | 15.98 (44.53)     | 0.004 <sup>a</sup>   |
| DELTA DIFF estimated TST at night, min    | 39.59 (70.95)                      | 12.85 (39.89)     | 0.0002 <sup>a</sup>  |
| DELTA DIFF estimated TST over 24 h, min   | 47.56 (78.52)                      | 16.03 (44.54)     | <0.0001 <sup>a</sup> |
| <b>Self-questionnaires</b>                |                                    |                   |                      |
| Epworth Sleepiness Scale total score      | 14.12 (4.81)                       | 14.86 (5.31)      | 0.003 <sup>a</sup>   |
| EQ-5D VAS                                 | 73.61 (14.53)                      | 67.02 (18.04)     | <0.0001 <sup>a</sup> |
| Narcolepsy Severity Scale total score     | 22.48 (10.06)                      | 22.01 (10.09)     | 0.63                 |

Abbreviations: DELTA DIFF = delta of the difference; EQ-5D = European Quality of life 5-dimensions questionnaire; TST = total sleep time; VAS = visual analog scale.

Continuous variables are expressed as numbers; mean (±SD).

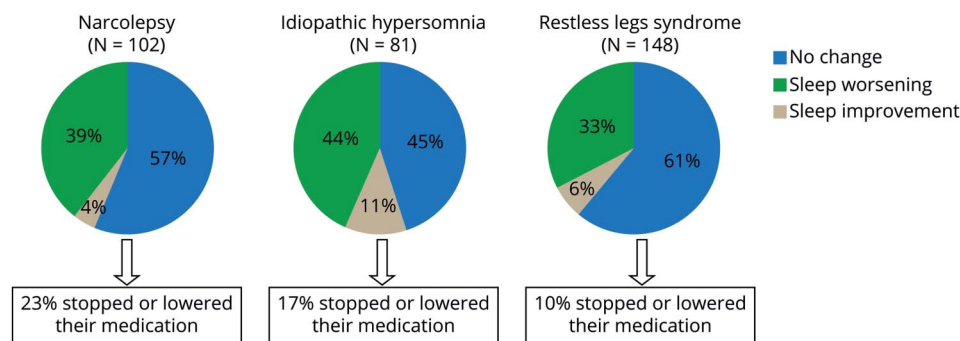
<sup>a</sup> Significance  $p < 0.05$ .

partial and generalized cataplexies and their consequences (based on 3 items of the NSS) did not differ significantly before and during the lockdown.

Fifty-three (56.38%) patients reported no effect of the lockdown on narcolepsy, 4 (4.26%) global improvement, and 37 (39.36%) worsening (Figure). Compared with prelockdown,

patients with narcolepsy worsening during the lockdown had more awakenings at night (weekends:  $2.79 \pm 2.29$  vs  $2.06 \pm 1.59$ ,  $p = 0.006$  and weekdays:  $2.39 \pm 1.97$  vs  $1.97 \pm 1.49$ ,  $p = 0.03$ ), increased total ESS scores ( $16.33 \pm 4.75$  vs  $15.00 \pm 4.29$ ,  $p = 0.04$ ), and lower QoL scores ( $59.44 \pm 14.62$  vs  $71.88 \pm 12.41$ ,  $p < 0.0001$ ). Comparing patients with and without narcolepsy worsening, we found no association with narcolepsy

**Figure** Effect of the Lockdown Situation on the Chronic Sleep Disease and Medication Intake in the 3 Groups



type (1 or 2), age, sex, occupational situation, modification of treatment, cataplexy frequency and consequences, and pre-lockdown NSS and BDI-II scores.

Before the lockdown, 93.14% of patients regularly took their treatment, and 90.20% during the lockdown. However, 25 (26.32%) modified their treatment during the lockdown: 3 stopped their medication, 20 lowered, and 2 increased the dosages. Compared with patients with stable/increased dosage, those who stopped/lowered their medication ( $n = 23$ ) were younger ( $31.74 \pm 15.47$  vs  $42.54 \pm 20.01$  years,  $p = 0.02$ ) and spent more time in bed (9 hours 40 minutes  $\pm$  1 hour 33 minutes vs 8 hours 50 minutes  $\pm$  1 hour 16 minutes,  $p = 0.02$ ), but no effect of diagnosis (NT1 or NT2), sex, occupational situation, and baseline NSS and BDI-II total scores was found. Compared with prelockdown, patients who stopped/lowered their treatment during the lockdown spent more time in bed (9 hours 09 minutes  $\pm$  1 hour 22 minutes vs 8 hours 26 minutes  $\pm$  1 hour 11 minutes,  $p = 0.03$ ), increased their TST over 24 hours during weekdays (8 hours 41 minutes  $\pm$  1 hour 59 minutes vs 7 hours 59 minutes  $\pm$  1 hour 25 minutes,  $p = 0.03$ ), and decreased their NSS total scores ( $17.92 \pm 6.53$  vs  $21.38 \pm 6.83$ ,  $p = 0.02$ ).

### Sleep Patterns in IH

During the lockdown, 25 (31.65%) patients with IH had a regular working schedule, 18 (22.78%) were working/studying at home, 8 (10.13%) off work, 12 (15.19%) partially unemployed/child caring, and 16 (20.25%) retired/unemployed. We found an increase in time spent in bed and TST overnight and over 24 hours on weekdays during the lockdown compared with baseline, without significant changes for weekend (Table 2). In both weekend and weekdays, bedtimes and wake-up times were delayed, and nocturnal sleep latency and number of awakenings increased during the lockdown. The differences between weekdays and weekends for bedtime, wake-up time, time spent in bed, and TST overnight and over 24 hours decreased during the lockdown (Table 2). No changes were found for ESS and IHSS total scores before vs during the lockdown, with a tendency for a lower EQ-5D score.

Twenty-eight (45.16%) patients reported no effect of lockdown on IH, 7 (11.29%) a global improvement, and 27 (43.55%) worsening (Figure). Compared with prelockdown, patients with IH worsening during the lockdown had longer nocturnal sleep latencies during weekends and weekdays ( $35.80 \pm 64.18$  vs  $7.16 \pm 8.44$  minutes,  $p = 0.0005$  and  $37.19 \pm 62.92$  vs  $8.62 \pm 12.69$  minutes,  $p < 0.0001$ ), more awakenings at night ( $2.63 \pm 4.21$  vs  $1.00 \pm 1.35$ ,  $p = 0.004$  and  $2.64 \pm 4.07$  vs  $0.96 \pm 1.34$ ,  $p = 0.002$ ), and worse QoL ( $56.11 \pm 21.47$  vs  $64.81 \pm 22.93$ ,  $p = 0.0003$ ). Compared with patients without IH worsening, those with worsening had a higher baseline IHSS total score ( $34.48 \pm 11.26$  vs  $27.09 \pm 8.49$ ,  $p = 0.01$ ), without association with age, sex, occupational situation, medication, and baseline BDI-II score. Before the lockdown, 61.73% regularly took their treatment, and 58.02% during the lockdown. Fourteen (28.00%) patients modified their treatment during the lockdown: 3 stopped their medication, and 11 lowered the dosages. No meaningful differences were found between patients with stable medication and those who stopped/lowered their medication. Compared with baseline, patients with IH who stopped/lowered their treatment during the lockdown spent more time in bed (10 hours 10 minutes  $\pm$  2 hours 22 minutes vs 8 hours 06 minutes  $\pm$  1 hour 18 minutes,  $p = 0.006$ ).

### Sleep Patterns in RLS

During the lockdown, 12 (8.45%) patients with RLS had a regular working schedule, 20 (14.08%) were working/studying at home, 9 (6.34%) off work, 6 (4.23%) partially unemployed/child caring, and 95 (66.90%) retired/unemployed. Compared with prelockdown, patients with RLS had longer sleep latency and more awakenings at night during lockdown weekdays and weekends. We also found more daytime naps in the weekdays and a decrease in time spent in bed and TST overnight and over 24 hours during the weekends' lockdown. RLS severity significantly increased, while QoL decreased, with no change in the ISI score (Table 3). During the lockdown, patients went to bed later during weekdays and weekends and woke up later in the weekdays only. The differences in bedtime, wake-up time,

**Table 2** Comparison of Sleep Habits and Self-Questionnaires Before and During the Lockdown in Patients With Idiopathic Hypersomnia

|   | Patients with idiopathic hypersomnia (N = 81) |                 | p Value              |
|---|---|-----------------|----------------------|
|   | Before lockdown                               | During lockdown |                      |
| <b>Sleep habits: weekdays</b>                     |   |                 |                      |
| Bed time, h:min                                   | 22:44 (1:00)                                  | 23:20 (1:29)    | <0.0001 <sup>a</sup> |
| Wake-up time, h:min                               | 7:14 (1:04)                                   | 8:29 (2:07)     | <0.0001 <sup>a</sup> |
| Time spent in bed, h:min                          | 8:30 (1:19)                                   | 9:09 (1:46)     | 0.0003 <sup>a</sup>  |
| Estimated TST at night, h:min                     | 8:17 (1:20)                                   | 8:55 (1:49)     | 0.002 <sup>a</sup>   |
| Night sleep latency, min                          | 11.06 (14.95)                                 | 21.41 (41.25)   | 0.0001 <sup>a</sup>  |
| No. of awakenings per night                       | 1.18 (2.00)                                   | 1.85 (3.11)     | 0.0004 <sup>a</sup>  |
| Presence of daytime napping, yes, n (%)           | 31 (40.26)                                    | 33 (42.86)      | 0.59                 |
| TST over 24 h, h:min                              | 8:42 (1:49)                                   | 9:20 (2:14)     | 0.003 <sup>a</sup>   |
| <b>Sleep habits: weekends</b>                     |   |                 |                      |
| Bed time, h:min                                   | 23:22 (1:07)                                  | 23:45 (1:29)    | 0.0006 <sup>a</sup>  |
| Wake-up time, h:min                               | 9:04 (1:31)                                   | 9:37 (1:50)     | <0.0001 <sup>a</sup> |
| Time spent in bed, h:min                          | 9:42 (1:39)                                   | 9:52 (1:39)     | 0.28                 |
| Estimated TST at night, h:min                     | 9:28 (1:36)                                   | 9:36 (1:39)     | 0.41                 |
| Night sleep latency, min                          | 9.85 (13.46)                                  | 20.16 (41.47)   | <0.0001 <sup>a</sup> |
| No. of awakenings per night                       | 1.14 (2.05)                                   | 1.85 (3.02)     | 0.002 <sup>a</sup>   |
| Presence of daytime napping, yes, n (%)           | 40 (51.95%)                                   | 38 (49.35%)     | 0.56                 |
| TST over 24 h, h:min                              | 10:07 (2:05)                                  | 10:11 (2:12)    | 0.57                 |
| <b>Sleep habits: weekdays vs weekends</b>         |   |                 |                      |
| DELTA DIFF bedtime, min                           | 38.80 (44.94)                                 | 25.60 (45.46)   | 0.004 <sup>a</sup>   |
| DELTA DIFF wake-up time, min                      | 110.40 (102.06)                               | 67.93 (90.72)   | 0.0004 <sup>a</sup>  |
| DELTA DIFF time spent in bed, min                 | 71.60 (92.78)                                 | 42.33 (75.63)   | 0.01 <sup>a</sup>    |
| DELTA DIFF estimated TST at night, min            | 70.44 (71.59)                                 | 41.40 (68.42)   | 0.001 <sup>a</sup>   |
| DELTA DIFF estimated TST over 24 h, min           | 85.04 (88.12)                                 | 51.69 (83.61)   | 0.0003 <sup>a</sup>  |
| <b>Self-questionnaires</b>                        |   |                 |                      |
| Epworth Sleepiness Scale total score              | 12.41 (5.37)                                  | 12.49 (5.34)    | 0.62                 |
| EQ-5D VAS   | 68.85 (20.26)                                 | 66.83 (20.38)   | 0.07                 |
| Idiopathic Hypersomnia Severity Scale total score | 28.13 (10.86)                                 | 28.48 (11.26)   | 0.96                 |

Abbreviations: DELTA DIFF = delta of the difference; EQ-5D = European Quality of life 5-dimensions questionnaire; TST = total sleep time; VAS = visual analog scale.

Continuous variables are expressed as numbers; mean (±SD).

<sup>a</sup> Significance  $p < 0.05$ .

time spent in bed, and TST over 24 hours between weekdays and weekends decreased during the lockdown (Table 3).

Eighty (61.07%) patients reported no effect of lockdown on their disease, 8 (6.11%) a global improvement, and 43 (32.82%) worsening (Figure). Compared with prelockdown, patients with RLS worsening during the lockdown had longer

sleep latency during weekends ( $45.84 \pm 51.25$  vs  $27.57 \pm 17.82$  minutes,  $p = 0.03$ ), more awakenings ( $4.38 \pm 5.57$  vs  $2.77 \pm 2.75$ ,  $p = 0.007$ ), decreased time spent in bed (7 hours 38 minutes ± 1 hour 54 minutes vs 8 hours 31 minutes ± 1 hour 23 minutes,  $p < 0.0001$ ), TST at night (5 hours 48 minutes ± 2 hours 07 minutes vs 7 hours 02 minutes ± 1 hour 48 minutes,  $p < 0.0001$ ), and TST over 24 hours (6 hours 17 minutes ± 2 hours 21

**Table 3** Comparison of Sleep Habits and Self-Questionnaires Before and During the Lockdown in Patients With Restless Legs Syndrome

|   | Patients with restless legs syndrome (N = 148) |                   | p Value              |
|---|--|-------------------|----------------------|
|   | Before lockdown                                | During lockdown   |                      |
| <b>Sleep habits: weekdays</b>             |  |                   |                      |
| Bed time, h:min                           | 23:05 (0:58)                                   | 23:28 (1:14)      | <0.0001 <sup>a</sup> |
| Wake-up time, h:min                       | 06:56 (1:19)                                   | 07:14 (1:46)      | <0.0001 <sup>a</sup> |
| Time spent in bed, h:min                  | 7:51 (1:20)                                    | 7:47 (1:36)       | 0.59                 |
| Estimated TST at night, h:min             | 6:26 (1:32)                                    | 6:17 (1:41)       | 0.15                 |
| Night sleep latency, min                  | 29.27 (24.75)                                  | 34.70 (37.26)     | 0.04 <sup>a</sup>    |
| No. of awakenings per night               | 2.50 (2.39)                                    | 2.69 (2.51)       | 0.05 <sup>a</sup>    |
| Presence of daytime napping, yes, n (%)   | 56 (40.88)                                     | 68 (49.64)        | 0.007 <sup>a</sup>   |
| TST over 24 h, h:min                      | 6:44 (1:39)                                    | 6:38 (1:37)       | 0.84                 |
| <b>Sleep habits: weekends</b>             |  |                   |                      |
| Bed time, h:min                           | 23:17 (0:59)                                   | 23:35 (1:14)      | <0.0001 <sup>a</sup> |
| Wake-up time, h:min                       | 07:30 (1:32)                                   | 07:30 (1:50)      | 0.42                 |
| Time spent in bed, h:min                  | 8:14 (1:27)                                    | 7:56 (1:41)       | 0.0006 <sup>a</sup>  |
| Estimated TST at night, h:min             | 6:42 (1:42)                                    | 6:23 (1:55)       | 0.01 <sup>a</sup>    |
| Night sleep latency, min                  | 28.43 (23.92)                                  | 35.17 (37.46)     | 0.02 <sup>a</sup>    |
| No. of awakenings per night               | 2.51 (2.41)                                    | 3.00 (3.60)       | 0.02 <sup>a</sup>    |
| Presence of daytime napping, yes, n (%)   | 66 (48.18)                                     | 71 (51.82)        | 0.17                 |
| TST over 24 h, h:min                      | 7:01:54 (1:45:40)                              | 6:46:27 (1:55:17) | 0.05 <sup>a</sup>    |
| <b>Sleep habits: weekdays vs weekends</b> |  |                   |                      |
| DELTA DIFF bedtime, min                   | 12.11 (28.30)                                  | 6.83 (21.73)      | 0.02 <sup>a</sup>    |
| DELTA DIFF wake-up time, min              | 34.05 (55.78)                                  | 16.04 (39.14)     | <0.0001 <sup>a</sup> |
| DELTA DIFF time spent in bed, min         | 22.10 (49.61)                                  | 9.28 (34.75)      | <0.0001 <sup>a</sup> |
| DELTA DIFF estimated TST at night, min    | 16.07 (43.22)                                  | 6.07 (44.18)      | 0.06                 |
| DELTA DIFF estimated TST over 24 h, min   | 17.66 (59.00)                                  | 7.98 (53.97)      | 0.03 <sup>a</sup>    |
| <b>Self-questionnaires</b>                |  |                   |                      |
| Epworth Sleepiness Scale total score      | 8.54 (5.66)                                    | 8.87 (6.01)       | 0.19                 |
| Insomnia Severity Index total score       | 13.43 (5.86)                                   | 14.05 (6.49)      | 0.13                 |
| EQ-5D VAS                                 | 68.09 (17.39)                                  | 63.94 (17.57)     | 0.0002 <sup>a</sup>  |
| IRLS total score                          | 19.83 (7.69)                                   | 20.66 (8.05)      | 0.02 <sup>a</sup>    |

Abbreviations: DELTA DIFF = delta of the difference; EQ-5D = European Quality of life 5-dimensions questionnaire; IRLS = International Restless Legs Syndrome Study Group questionnaire; TST = total sleep time; VAS = visual analog scale.

Continuous variables are expressed as numbers; mean (±SD).

<sup>a</sup> Significance  $p < 0.05$ .

minutes vs 7 hours 21 minutes ± 2 hours 05 minutes,  $p < 0.0001$ ), with significant differences also observed during the weekdays (data not shown). They also had increased ESS ( $11.00 \pm 6.65$  vs  $9.24 \pm 5.65$ ,  $p = 0.002$ ), ISI ( $17.85 \pm 5.75$  vs  $14.95 \pm 5.52$ ,  $p = 0.002$ ), and IRLS total scores ( $24.34 \pm 7.57$  vs  $20.43 \pm$

$6.69$ ,  $p < 0.0001$ ) and lower QoL scores ( $57.45 \pm 18.63$  vs  $67.67 \pm 19.45$ ,  $p = 0.0002$ ) during the lockdown compared with pre-lockdown. Compared with patients without RLS worsening, those with worsening were younger ( $56.42 \pm 12.69$  vs  $63.50 \pm 12.42$  years,  $p = 0.004$ ) and had a higher baseline BDI-II total

score ( $15.38 \pm 7.57$  vs  $10.36 \pm 9.59$ ,  $p = 0.007$ ), but no differences were found for sex, occupational situation, modification of treatment, and baseline IRLS and ISI total scores.

Before the lockdown, 72.97% patients regularly took their RLS treatment, and 66.22% during the lockdown. Twenty-four (22.22%) patients modified their medication during the lockdown: 10 stopped their medication, 4 lowered, and 10 increased the dosages. Stopping/lowering medication was not associated with age, sex, occupational situation, and baseline IRLS, BDI-II, and ISI total scores. However, those who lowered/stopped their treatment increased their TST at night (7 hours 25 minutes  $\pm$  1 hour 04 minutes vs 6 hours 45 minutes  $\pm$  1 hour 16 minutes,  $p = 0.02$ ) and over 24 hours during the weekdays (7 hours 33 minutes  $\pm$  1 hour 05 minutes vs 6 hours 59 minutes  $\pm$  1 hour 18 minutes,  $p = 0.03$ ) during the lockdown compared with prelockdown. Patients who increased the dose of their drugs ( $n = 10$ ,  $63.50 \pm 9.91$  years old, 50% women, half with dopamine agonists alone, half with dopamine agonists in combination) reported no significant differences in QoL, ESS, ISI, and IRLS total scores between the 2 conditions.

## Discussion

We explored the effects of the first COVID-19 lockdown in France on sleep and related symptoms in patients with a chronic neurologic sleep disorder (narcolepsy, IH, and RLS). All patients reported later bedtimes with reduced differences for time in bed and total TST over 24 hours between weekdays and weekends. Patients with narcolepsy and IH spent more time in bed and increased TST overnight, but the opposite was observed in patients with RLS. We found more daytime napping and higher ESS scores in narcolepsy but not in IH, and patients with RLS reported more naps with no ESS changes. All patients reported more awakenings at night, and increased nocturnal sleep latencies were found in IH and RLS. The severity of the diseases assessed with validated scales increased in RLS but not in narcolepsy or in IH. However, a significant proportion of patients reported worsening of disease burden (39.4% narcolepsy, 43.6% IH, and 32.8% RLS) during the lockdown, and some patients stopped or lowered spontaneously their medication (22.5% narcolepsy, 28% IH, and 9.5% RLS). QoL significantly decreased in narcolepsy and RLS, with a similar tendency in IH.

The COVID-19 pandemic has changed people's lives considerably, with unprecedented modifications in social, work, travel, and leisure activities. During the lockdown, schools and universities were closed, and access to public places was limited. People had reduced physical activity and daylight exposure and a lack of social zeitgebers, with no fixed work schedule. Social isolation, home confinement, and loneliness were associated worldwide with a multitude of health problems, such as psychological distress (anxiety, depression, and suicidal ideation) and sleep disturbances.<sup>1-7</sup> The lockdown effects on sleep in the

general population were studied in several countries, with international studies conducted. In a large-scale survey, participants reported poor sleep quality, sleep onset and sleep maintenance problems, increased nightmares, hypnotic use, fatigue, and excessive sleepiness.<sup>4</sup> In another study, most participants exhibited a reduction of their social jetlag, with later sleep timing, but more insomnia.<sup>5</sup> Other studies also showed delayed bedtimes and wake-up times, more time spent in bed, and poorer sleep quality in young adults, with more changes in those with higher levels of depression, anxiety, and stress.<sup>29</sup> More insomnia disorders, especially in women and younger age groups, were also reported in a third collaborative study.<sup>6</sup>

The effect of quarantine in patients with chronic neurologic sleep disorders has been understudied. Such changes in environment, social habits, and stressful conditions may have modified the disease burden with different baseline sleep phenotypes: sleepiness and often DNS in narcolepsy,<sup>30,31</sup> sleepiness and prolonged nocturnal sleep in IH,<sup>10</sup> and insomnia in RLS.<sup>32</sup> In narcolepsy during confinement, there are discrepancies across the few published data across countries, with either improvement or worsening of the symptoms.<sup>15-18,33</sup> A sample of patients with narcolepsy in China did not report disease worsening, even when they discontinued their treatment,<sup>15</sup> whereas another study in Brazil showed worsening of all narcolepsy symptoms.<sup>17</sup> In Italy, patients working/studying at home extended their nocturnal sleep and had less sleepiness.<sup>16</sup> Another study showed later bed and wake-up time and increased sleep but no differences for sleep quality and sleepiness in NT1 children evaluated by actigraphy.<sup>33</sup> In a recent web survey in France, one-third of patients with narcolepsy and IH increased their nighttime sleep and improved sleepiness, especially teleworkers, and cataplexy improved in 54% of patients with NT1.<sup>18</sup> We found that patients with narcolepsy and IH increased their time spent in bed and TST but had more awakenings at night, in line with previous studies.<sup>16-18,33</sup> Nocturnal sleep latencies increased in IH but not in narcolepsy, with more naps in narcolepsy but not in IH. Subjective sleepiness and complaint of DNS increased in narcolepsy, while QoL decreased. Conversely, sleepiness and QoL did not change significantly in IH. In both samples, the global severity of the disease assessed with the NSS and IHSS, respectively, did not change. In our study, the cataplexy frequency and their consequences did not change. A substantial proportion of patients reported, however, worsening of disease burden (39.4% narcolepsy and 43.6% IH) during the lockdown, with more awakenings at night, lower QoL in both conditions, and increased ESS scores in only narcolepsy. The lack of daily activity could explain sleepiness worsening in narcolepsy. During the lockdown, they could sleep at will but were also most of the time in a state of inactivity or quiet activity, facilitating drowsiness, and patients with narcolepsy do not have a 24-hour excessive amount of sleep, but rather an inability to stay awake or asleep for a long time. Patients with IH did not behave the same way: their increase in the amount of sleep over 24-hour is often incompatible with their regular social and working activities. During the lockdown, with less time constraints, they could increase their sleep time, and their sleepiness did not worsen. Compared with patients with narcolepsy, they might



also be affected with a less severe condition and could better adapt their symptoms to their occupations.

Patients with RLS responded to the survey with a fairly high frequency, as the situation was possibly more stressful for them, being older and therefore more at risk of COVID-19 infection. Patients with RLS had longer sleep latency and more awakenings during the lockdown and even more so in patients with disease worsening (32.8%). Patients went to bed and woke up later with subsequent insomnia symptoms. RLS severity and sleepiness increased while QoL worsened during the lockdown, which was more pronounced in the subgroup with disease worsening. The increased daytime napping could be either a cause (more nap opportunities due to fewer constraints) or a consequence of worsening in RLS severity and related disturbed nighttime sleep. Sleep worsening was associated with younger age and more depressive symptoms before the lockdown. In another French survey, people with depressive symptoms also reported sleep worsening during the lockdown,<sup>34</sup> and we recently showed that depression is associated with RLS and relates to insomnia symptoms, younger age, and female sex, with frequent suicidal thoughts.<sup>35</sup>

Almost all patients with narcolepsy (90.20%) reported a regular intake of medication during the lockdown, but only 58.02% in patients with IH and 66.22% in patients with RLS, with similar results before the lockdown. Moreover, a substantial group of patients with narcolepsy (22.5%) stopped/lowered their medication: they were younger, spent more time in bed, increased their TST over 24 hours during weekdays, and had lower NSS total scores compared with patients with stable treatment. These results suggest that some young patients with narcolepsy are chronically sleep deprived and may benefit from nighttime sleep extension and daytime naps, as often recommended in non-pharmacologic management.<sup>13</sup> Several patients with IH (28%) also stopped/lowered their medication during the lockdown. They spent more time in bed, and had a longer nocturnal sleep latency during weekdays. Between weekdays and weekends, they showed reduced differences of time spent in bed, TST overnight, and TST over 24 hours. Finally, they perceived their disease as less severe. As in narcolepsy, these results suggest that some patients with IH may clinically benefit from prolonged sleep, with a debate still lively on a possible continuum between IH and long sleepers.<sup>36,37</sup> In contrast, a low percentage of patients with RLS stopped/lowered medication. They increased their TST during the weekdays, but insomnia and RLS symptoms eventually worsened. Ten patients with RLS increased their drug dosage (all took DA), a condition at risk for augmentation syndrome and impulse control disorder that should be carefully monitored over the long term.<sup>32</sup>

Our study was not designed to compare the 3 groups with each other, but we can observe that they behaved differently during the lockdown, probably because of different sleep phenotypes at baseline, different age ranges and sex ratios, which could influence sleep habits and occupations. Moreover, the usual differences between weekdays and weekends, being proxy markers of sleep

timing and sleep deprivation, disappeared during the lockdown with potentially different effects in these 3 disorders. Also, patients with RLS were less prone to stop spontaneously their medication because their main symptom is an urge to move the legs at night, often painful or uncomfortable, whereas in central disorders of hypersomnolence, the social consequences of sleepiness may be sometimes more bothersome than the symptom itself.

Since this first lockdown, teleconsultations have been organized more systematically to monitor patients diagnosed in our sleep disorders center, as in other centers worldwide. Physicians can recommend their patients better sleep hygiene, more suitable sleep schedules, extended sleep at night, and scheduled daytime naps as well as monitor medications and doses and prevent complications. During these teleconsultations, they can detect worsening of the disease, poor QoL, and increased levels of stress, anxiety, depressive symptoms, or even suicidal thoughts,<sup>35,38</sup> potentially linked to the psychological effects of confinement.

Among the strengths of our study, we used standardized evaluations, specific validated questionnaires, and we included only well-characterized patients. Overall, the present data constitute one of the largest collections of patients with central disorders of hypersomnolence studied for sleep symptoms during the lockdown and the first study of patients with RLS during the lockdown. We also acknowledge some limitations. We included patients with 3 neurologic sleep disorders, which may not be representative of these disorders (response rate of 40.71%) or of the consequences of confinement on other sleep or neurologic diseases. Our results may also be specific to France because each country has responded differently to the pandemic. We did not include a control group to assess the specificities of the associations. The study design may introduce a recall bias, but it also allows a homogeneous evaluation, with similar sleep assessment. It included data from weekdays and weekends, and over a similar period: 1 month before the lockdown and during the lockdown. It also allowed a closer time period of evaluation, just before the confinement. Also, patients completed the questionnaire only during the first lockdown, and their sleep habits and sleep symptoms may have changed over time. Data on stress, anxiety, circadian problems, and daily physical activity were lacking, as well as environmental factors such as daily exposure to natural sunlight. The size of some subgroups (teleworkers and patients who stopped medication) was too small to perform further analyses and between-group comparisons. Our study did not focus on COVID-19 infection, and very few patients had been tested for COVID-19 at that time in France.

To summarize, our study on narcolepsy, IH, and RLS showed the key effect of the first lockdown due to COVID-19, with an extension of sleep duration for narcolepsy and IH, unlike RLS, and changes often associated with negative consequences on QoL. A significant portion of patients reported overall disease worsening, while some patients

stopped/lowered their medications. Changes in the environment, social habits, and stressful situations can have direct effects on sleep symptoms and disease burden with wide variations among patients. The recent development of teleconsultations should enable physicians to monitor patients with chronic sleep disorders more closely, to recommend optimized sleep schedules and duration, to prevent psychological problems, and improve their QoL.

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L. Barateau received honoraria for speaking from UCB Pharma and Jazz, board engagements from UCB Pharma, Jazz, Bioprojet, and Takeda, and travel to congress from Laidet Medical and UCB Pharma. Y. Dauvilliers received honoraria for speaking and board engagements from UCB Pharma, Jazz, Bioprojet, Theranexus, Takeda, and Idorsia. R. Lopez received honoraria for speaking from UCB Pharma and Shire and travel to congress from Laidet Medical. The other authors report no relevant disclosures. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

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## Changes in Sleep Pattern During the COVID-19 Lockdown in Patients With Narcolepsy, Idiopathic Hypersomnia, and Restless Legs Syndrome

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