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 COVID-19 lockdown impact 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, 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 pre-lockdown (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-24h between weekdays and weekends. Narcoleptic patients spent more TIB and increased TST overnight, with more daytime napping. They had more awakenings, higher ESS scores, lower QoL, and no NSS changes. IH patients had also increased TIB, TST overnight and 24-h on weekdays. Nocturnal sleep latency and number of awakenings increased, but with no change in ESS, QoL, and IHSS scores. RLS patients reported a longer nocturnal sleep latency, more awakenings, more naps, a decreased TIB and TST overnight. RLS severity increased while QoL decreased. A significant portion of patients reported disease worsening during lockdown (narcolepsy:39.4%, IH:43.6%, RLS:32.8%), and some patients stopped or lowered their medication (narcolepsy:22.5%, IH:28%, RLS:9.5%).
**Conclusion:** During the lockdown, all patients reported later bedtimes; those with narcolepsy and IH extended their sleep duration unlike RLS patients. 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, to recommend optimized sleep schedules and duration, in order to prevent psychological problems and improve their QoL.

**INTRODUCTION**

The forced social and work distancing during the coronavirus disease (COVID-19) pandemic lockdown led to several health-related problems such as mood, psychological disturbances, and sleep troubles in the general population.\(^1\)–\(^3\) Whether this exceptional situation had similar impact on patients with sleep disorders remains unclear and controversial.\(^4\)–\(^7\) 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.\(^8\) In narcolepsy, excessive daytime sleepiness is severe and nocturnal sleep has usually a normal duration but is fragmented.\(^9\) In contrast, IH is characterized by a prolonged undisrupted nocturnal sleep with long unrefreshing naps, and often sleep inertia.\(^10\) 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.\(^11\) Management of these disorders requires first a non-pharmacological approach with good sleep hygiene recommendations, and medication for moderate to severe cases.\(^12\)–\(^14\)

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. While 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\textsuperscript{15–18}; and only one included patients with IH.\textsuperscript{18}
Moreover, weekdays and weekends sleep habits before 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 lockdown.

This unique extreme situation that lasted three months in France provided an
opportunity to assess the evolution of symptoms of patients suffering from chronic
neurological sleep disorders, as well as 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 three
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 the 17\textsuperscript{th} March and the 11\textsuperscript{th} May 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 one hour per day, in a limited area around the
residence. Hospitalizations and consultations of 813 adult patients suffering from narcolepsy,
IH, or RLS were cancelled 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 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 impact 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 and Patient Consent

This project was approved by the local ethics committees (Institutional Review Board,
Montpellier University Hospital, France). All patients gave consent for use of their answers in
this publication. This study is ancillary to the SOMNOBANK project ("Constitution of a
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, medication intake, with several validated and dedicated scales for sleep symptoms and the three different diseases. The survey was proposed once to the patients, and the questions were answered for the pre-lockdown (recall of the month before the confinement) and the lockdown (time of study) periods. Daily activities or current working status was recorded and categorized as (1) regular working schedule; (2) working/studying at home; (3) sick-leave; (4) partial unemployment or child care; (5) unemployed or retired. Similar 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-h, sleep onset latency, number of awakenings, 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 impact on their sleep disease (no perceived effect/improvement/worsening). Current medication for narcolepsy, IH and RLS was recorded. All patients were asked to report if 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).\textsuperscript{19} QoL before and during the lockdown was assessed with the European QoL five-dimensions (EQ-5D) visual analog scale (VAS) scores, with higher scores indicating better QoL.\textsuperscript{20} The presence and severity of depressive symptoms during the last two weeks before the lockdown were evaluated with the Beck Depression Inventory-II (BDI-II).\textsuperscript{21} To assess the severity of their symptoms before and during the lockdown, patients with narcolepsy completed the Narcolepsy Severity Scale (NSS)\textsuperscript{22,23} (with one item on disrupted nocturnal sleep (DNS) complaint, and three items on partial and generalized cataplexy frequencies and their consequences, further analyzed independently), patients with IH completed the Idiopathic Hypersomnia Severity Scale (IHSS),\textsuperscript{24} and patients with RLS completed the International RLS Study Group questionnaire (IRLS)\textsuperscript{25} and the Insomnia Severity Index (ISI)\textsuperscript{26} to assess related insomnia symptoms.

The complete survey in its original French language is available in the supplemental material.
**Statistical analyses**

Demographic and clinical characteristics were described using means and standard deviations for continuous variables or number and percentages for categorical variables. Comparisons between two evaluations (before and during the lockdown) were performed using the Wilcoxon signed-rank test for continuous variables and Mc Nemar’s test or Bowkers’ 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 Statement.** The data that support this study findings are available from the corresponding authors, upon reasonable request.

**RESULTS**

**Participants’ characteristics**

Overall, 331 patients were included (response rate 40.71%; 64.65% women, mean age 48.60±19.24 years): 102 with narcolepsy (88 NT1, 14 NT2), 81 with IH and 148 with RLS.

In the 102 patients with narcolepsy (60.78% women), the mean age was 40.11±19.54 years. Diagnosis of NT1 and NT2 was previously confirmed based on the 3rd International Classification of Sleep Disorders (ICSD-3) criteria\(^{27}\) with a baseline mean sleep latency on the Multiple Sleep Latency Test (MSLT) at 5.26±3.65 min, with 3.46±1.21 sleep-onset REM periods. HLA genotyping was available for 94 patients (81 NT1, 13 NT2), all NT1 and 9 NT2 carried the allele DQB1*06:02. Cerebrospinal (CSF) orexin-A levels were measured for 74 NT1 (mean levels 27.42±25.76 pg/mL, all <110 pg/mL) and 11 NT2 (mean levels 259.27±79.95 pg/mL; eight patients >200 pg/mL and three with intermediate levels).

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

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

**Sleep patterns in narcolepsy**

During the lockdown, 13 (13.83%) narcoleptic patients 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-hour with more frequent naps on weekdays during lockdown compared with pre-lockdown, without significant changes for the weekend period (TABLE 1). In both weekend and weekdays, number of awakenings increased during the lockdown period. Patients reported later bedtimes during both weekdays and week-ends, and later wake-up times on weekends only. The differences between weekdays/weekends of bedtime, wake-up time, time spent in bed, TST overnight and TST over-24h highly decreased during lockdown (TABLE 1). Compared to pre-lockdown, ESS total scores were higher during lockdown, with lower QoL score, without significant changes for NSS, except for an increased in DNS (43.01% vs 35.48% with moderate/severe DNS, p=0.03). The frequency of partial and generalized cataplexies and their consequences (based on 3 items of NSS) did not differ significantly before and during lockdown.

Fifty-three (56.38%) patients reported no impact of the lockdown on narcolepsy, 4 (4.26%) a global improvement, and 37 (39.36%) a worsening (FIGURE 1). Compared to pre-lockdown, patients with narcolepsy worsening during lockdown had more awakenings at night (weekends: 2.79±2.29 vs 2.06±1.59, p=0.006 and weekdays: 2.39±1.97 vs 1.97±1.49, p=0.03), increased total ESS scores (16.33±4.75 vs 15.00±4.29, p=0.04) and lower QoL scores (59.44±14.62 vs 71.88±12.41, p<0.0001). Comparing patients with and without narcolepsy worsening, we found no association with narcolepsy type (1 or 2), age, gender, occupational situation, modification of treatment, cataplexy frequency and consequences, and pre-lockdown NSS and BDI-II scores.

Before lockdown, 93.14% of patients regularly took their treatment, and 90.20% during lockdown. However, 25 (26.32%) modified their treatment during the lockdown: 3
stopped their medication, 20 lowered and 2 increased the dosages. Compared to patients with stable/increased dosage, those who stopped/lowered their medication (n=23) were younger (31.74±15.47 vs 42.54±20.01 y.o., p=0.02), and spent more time in bed (9h40min±1h 33min vs 8h50min±1h16min, p=0.02), but no effect of diagnosis (NT1 or NT2), gender, occupational situation, and baseline NSS and BDI-II total scores were found. Compared to pre-lockdown, patients who stopped/lowered their treatment during lockdown spent more time in bed (9h09min±1h22min vs 8h26min±1h11min, p=0.03), increased their TST over 24-hour during weekdays (8h41min±1h59min vs 7h59min±1h25min, p=0.03), and decreased their NSS total scores (17.92±6.53 vs 21.38±6.83, p=0.02).

Sleep patterns in idiopathic hypersomnia

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-hour on weekdays during 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-24h decreased during lockdown (TABLE 2). No changes were found for ESS and IHSS total scores before vs during lockdown, with a tendency for a lower EQ-5D score.

Twenty-eight (45.16%) patients reported no impact of lockdown on IH, 7 (11.29%) a global improvement, and 27 (43.55%) a worsening (FIGURE 1). Compared to pre-lockdown, patients with IH worsening during lockdown had longer nocturnal sleep latencies during weekends and weekdays (35.80±64.18 vs 7.16±8.44 min, p=0.0005 and 37.19±62.92 vs 8.62±12.69 min, p<0.0001), more awakenings at night (2.63±4.21 vs 1.00±1.35, p=0.004 and 2.64±4.07 vs 0.96±1.34, p=0.002), and worse QoL (56.11±21.47 vs 64.81±22.93, p=0.0003). Compared to patients without IH worsening, those with worsening had higher baseline IHSS total score (34.48±11.26 vs 27.09±8.49, p=0.01), without association with age, gender, occupational situation, medication, and baseline BDI-II score. Before lockdown, 61.73% regularly took their treatment, and 58.02% during lockdown. Fourteen (28.00%) patients modified their treatment during 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 to baseline, patients with IH who
stopped/lowered their treatment during lockdown spent more time in bed (10h10min±2h22min vs 8h06min±1h18min, p=0.006).

Sleep patterns in restless legs syndrome

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 to pre-lockdown, patients with RLS had a 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 spend in bed and TST overnight and over 24-hour during the weekends’ lockdown. RLS severity significantly increased, while QoL decreased, with no change on ISI score (TABLE 3). During lockdown, patients went to bed later during weekdays and weekends, and woke-up later in the weekdays only. The differences on bedtime, wake-up time, time spent in bed and TST over-24h between weekdays and weekends decreased during lockdown (TABLE 3).

Eighty (61.07%) patients reported no impact of lockdown on their disease, 8 (6.11%) a global improvement, and 43 (32.82%) a worsening (FIGURE 1). Compared to pre-lockdown, patients with RLS worsening during lockdown had a longer sleep latency during weekends (45.84±51.25 vs 27.57±17.82 min, p=0.03), more awakenings (4.38±5.57 vs 2.77±2.75, p=0.007), decreased time spent in bed (7h38min±1h54min vs 8h31±1h23min, p<0.0001), TST at night (5h48min±2h07min vs 7h02min±1h48min, p<0.0001) and TST over 24-hour (6h17min±2h21min vs 7h21min±2h05min, p<0.0001), with significant differences also observed during the weekdays (data not shown). They also had increased ESS (11.00±6.65 vs 9.24±5.65, p=0.002), ISI (17.85±5.75 vs 14.95±5.52, p=0.002) and IRLS total scores (24.34±7.57 vs 20.43±6.69, p <0.0001) and lower QoL scores (57.45±18.63 vs 67.67±19.45, p=0.0002) during lockdown compared to pre-lockdown. Compared to patients without RLS worsening, those with worsening were younger (56.42±12.69 vs 63.50±12.42 y.o., p=0.004), and had higher baseline BDI-II total score (15.38±7.57 vs 10.36±9.59, p=0.007), but no differences were found for gender, occupational situation, modification of treatment, and baseline IRLS and ISI total scores.

Before lockdown, 72.97% patients regularly took their RLS treatment, and 66.22% during 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, gender, occupational situation,
and baseline IRLS, BDI-II and ISI total scores). However, those who lowered/stopped their treatment increased their TST at night ($7h25min±1h04min \text{ vs } 6h45min±1h16min$, p=0.02) and over 24h during the weekdays ($7h33min±1h05min \text{ vs } 6h59min±1h18min$, p=0.03) during the lockdown compared to pre-lockdown. Patients who increased the dose of their drugs (n=10, 63.50±9.91 y.o., 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 two conditions.

**DISCUSSION**

We explored the effects of the first COVID-19 lockdown in France on sleep and related symptoms in patients with a chronic neurological sleep disorder (narcolepsy, IH, and RLS). All patients reported later bedtimes with reduced differences for time in bed and total TST over-24h between weekdays and weekends. While patients with narcolepsy and IH spent more time in bed and increased TST overnight, the opposite was observed in patients with RLS. We found more daytime napping and higher ESS scores in narcolepsy, but not in IH; and RLS patients 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 nor in IH. However, a significant proportion of patients reported a worsening of disease burden (39.4% narcolepsy, 43.6% IH, 32.8% RLS) during the lockdown, and some patients stopped or lowered spontaneously their medication (22.5% narcolepsy, 28% IH, 9.5% RLS). QoL significantly decreased in narcolepsy and RLS, with a same tendency in IH.

The COVID-19 pandemic has changed people’s lives considerably, with unprecedented modifications in social, work, travel, and leisure activities. During lockdown, schools and universities were closed, access to public places limited. People had a reduced physical activity and daylight exposure, and a lack of social *zeitgebers*, with no fixed work schedule. Social isolation, home confinement and loneliness was associated worldwide with a multitude of health problems, such as psychological distress (anxiety, depression, suicidal ideation), and sleep disturbances.\(^1\)\(^-\)\(^7\) 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.\(^4\) In another study most participants exhibited a reduction of their social jetlag, with later sleep timing; but more insomnia.\(^5\) 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. More insomnia disorders, especially in women and younger age groups, were also reported in a third collaborative study.

The effect of quarantine in patients with chronic neurological 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 disrupted nocturnal sleep in narcolepsy, sleepiness and prolonged nocturnal sleep in IH, insomnia in RLS. In narcolepsy during confinement, there are discrepancies across the few published data across countries, with either improvement or worsening of the symptoms. A sample of narcoleptic patients in China did not report disease worsening, even when they discontinued their treatment, while another study in Brazil showed a worsening of all narcolepsy symptoms. In Italy, patients working/studying at home extended their nocturnal sleep and had less sleepiness. Another study showed later bed and wake up time, increased sleep, but no differences for sleep quality and sleepiness in NT1 children evaluated by actigraphy. 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 NT1 patients. 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. 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 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 a worsening of disease burden (39.4% narcolepsy and 43.6% IH) during the lockdown, with increased number of awakenings at night, lower QoL in both conditions, and increased ESS scores in narcolepsy only. The lack of daily activity could explain sleepiness worsening in narcolepsy. During lockdown they could sleep at will, but were also most of the time in a state of inactivity or quiet activity, facilitating drowsiness; and narcoleptic patients do not have a 24-h excessive amount of sleep, but rather an inability to stay awake or asleep for a long time. IH patients did not behave the same way: their increase amount of sleep over 24-h is often incompatible with their regular social and working activities. During lockdown, with less time constraints, they could increase their sleep time and their sleepiness did not worsen.
Compared to narcoleptic patients, 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 possibly more stressful for them, being older and therefore more at risk of COVID-19 infection. Patients with RLS had a 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, that was more pronounced in the subgroup with disease worsening. The increased daytime napping could be either a cause (more nap opportunities due to less constraints) or a consequence of a worsening in RLS severity and related disturbed nighttime sleep. Sleep worsening was associated with younger age and more depressive symptoms before lockdown. In another French survey, people with depressive symptoms also reported sleep worsening during the lockdown, and we recently showed that depression is associated with RLS and relates to insomnia symptoms, younger age and female gender, with frequent suicidal thoughts.

Almost all patients with narcolepsy (90.20%) reported a regular intake of medication during the lockdown, but only 58.02% in IH, and 66.22% in RLS patients, with similar results before lockdown. Moreover, a substantial group of patients with narcolepsy (22.5%) in our study stopped/lowered their medication: they were younger, spent more time in bed, increased their TST over 24-hour during weekdays and had lower NSS total scores compared to 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-pharmacological management. Several patients with IH (28%) also stopped/lowered their medication during lockdown. They spent more time in bed, had a longer nocturnal sleep latency in weekdays, with reduced differences on time spent in bed, TST overnight and over-24h between weekdays and weekends, and finally 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. 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. In contrast, ten RLS patients 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.
Our study was not designed to compare the three groups with each other, but we can observe that they behaved differently during lockdown, probably due to different sleep phenotypes at baseline, different age ranges and sex ratio, that 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 lockdown with potentially different impact in these three disorders. Also, RLS patients were less prone to stop spontaneously their medication, as 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 a 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 a worsening of the disease, a poor QoL and an increase in the levels of stress, anxiety, depressive symptoms, or even suicidal thoughts,\textsuperscript{35,38} 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 collection of patients with central disorders of hypersomnolence ever studied for sleep symptoms during lockdown, and the first study of RLS patients during lockdown. We acknowledged also some limitations. We included patients with three neurological sleep disorders, that may not be representative of these disorders (response rate of 40.71%) nor of the consequences of confinement on other sleep or neurological diseases. Our results may also be specific to France, as each country has responded differently to the pandemic. We did not include control subjects to assess the specificities of the associations. Our study design may have introduced recall bias, but also allows a homogeneous evaluation between patients with similar sleep assessment, including data from weekdays and weekends, and over a similar period (one month before lockdown and during lockdown, time of study), and also a closer time-period of evaluation, just before the confinement. Also, patients only completed the questionnaire during the first lockdown, and their sleep habits and sleep symptoms may have changed over time. Data on stress, anxiety, circadian problems, daily physical activity were lacking, as well as environmental factors such as daily exposure to
natural sunlight. The size of some subgroups (tele-workers, 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 impact 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 an 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 better follow patients suffering from chronic sleep disorders, to recommend optimized sleep schedules and duration, to prevent psychological problems and improve their QoL.

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FIGURES AND TABLES

FIGURE 1. Effect of the lockdown situation on the chronic sleep disease and medication intake in the three groups.
**TABLE 1.** Comparison of sleep habits and self-questionnaires before and during lockdown in patients with narcolepsy.

<table>
<thead>
<tr>
<th>PATIENTS WITH NARCOLEPSY N=102</th>
<th>Before lockdown</th>
<th>During lockdown</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep habits - Weekdays</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed time, hour:min</td>
<td>22:48 (0:55)</td>
<td>23:23 (1:12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Wake-up time, hour:min</td>
<td>07:04 (1:05)</td>
<td>07:59 (1:36)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time spent in bed, hour:min</td>
<td>8:17 (1:12)</td>
<td>8:37 (1:26)</td>
<td>0.01</td>
</tr>
<tr>
<td>Estimated TST at night, hour:min</td>
<td>7:28 (1:32)</td>
<td>7:47 (1:47)</td>
<td>0.01</td>
</tr>
<tr>
<td>Night sleep latency, min</td>
<td>8.51 (7.50)</td>
<td>9.36 (10.23)</td>
<td>0.33</td>
</tr>
<tr>
<td>Number of awakenings per night</td>
<td>2.20 (1.89)</td>
<td>2.47 (1.19)</td>
<td>0.03</td>
</tr>
<tr>
<td>Presence of daytime napping, yes (n, %)</td>
<td>74 (79.57 %)</td>
<td>82 (88.17 %)</td>
<td>0.02</td>
</tr>
<tr>
<td>TST over 24h, hour:min</td>
<td>7:53 (1:31)</td>
<td>8:23 (1:49)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Sleep habits - Weekends</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed time, hour:min</td>
<td>23:25 (0:59)</td>
<td>23:40 (1:12)</td>
<td>0.02</td>
</tr>
<tr>
<td>Wake-up time, hour:min</td>
<td>08:26 (1:31)</td>
<td>08:31 (1:35)</td>
<td>0.25</td>
</tr>
<tr>
<td>Time spent in bed, hour:min</td>
<td>9:03 (1:22)</td>
<td>8:53 (1:25)</td>
<td>0.10</td>
</tr>
<tr>
<td>Estimated TST at night, hour:min</td>
<td>8:07 (1:54)</td>
<td>8:00 (1:54)</td>
<td>0.37</td>
</tr>
<tr>
<td>Night sleep latency, min</td>
<td>9.08 (10.19)</td>
<td>9.33 (10.51)</td>
<td>0.86</td>
</tr>
<tr>
<td>Number of awakenings per night</td>
<td>2.05 (1.83)</td>
<td>2.68 (3.61)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Presence of daytime napping, yes (n, %)</td>
<td>79 (84.95 %)</td>
<td>82 (88.17 %)</td>
<td>0.26</td>
</tr>
<tr>
<td>TST over 24h, hour:min</td>
<td>8:40:42 (1:59:23)</td>
<td>8:38:57 (1:57:48)</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>Sleep habits - Weekdays vs Weekends</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DELTA DIFF bedtime, min</td>
<td>37.17 (52.68)</td>
<td>16.25 (30.52)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
DELTA DIFF wake-up time, min  |  82.31 (91.03)  |  31.88 (53.97)  |  <0.0001  
DELTA DIFF Time spent in bed, min  |  46.03 (72.73)  |  15.98 (44.53)  |  0.004  
DELTA DIFF Estimated TST at night, min  |  39.59 (70.95)  |  12.85 (39.89)  |  0.0002  
DELTA DIFF Estimated TST over 24h, min  |  47.56 (78.52)  |  16.03 (44.54)  |  <0.0001  

**Self-questionnaires**

Epworth sleepiness scale total score  |  14.12 (4.81)  |  14.86 (5.31)  |  0.003  
EQ-5D VAS  |  73.61 (14.53)  |  67.02 (18.04)  |  <0.0001  
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 five-dimensions questionnaire, TST = total sleep time, VAS = visual analog scale.
Continuous variables are expressed as numbers; means (± standard deviation)

**TABLE 2.** Comparison of sleep habits and self-questionnaires before and during lockdown in patients with idiopathic hypersomnia.

<table>
<thead>
<tr>
<th>PATIENTS WITH IDIOPATHIC HYPERSOMNIA N=81</th>
<th>Before lockdown</th>
<th>During lockdown</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep habits - Weekdays</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed time, hour:min</td>
<td>22:44 (1:00)</td>
<td>23:20 (1:29)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Wake-up time, hour:min</td>
<td>7:14 (1:04)</td>
<td>8:29 (2:07)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time spent in bed, hour:min</td>
<td>8:30 (1:19)</td>
<td>9:09 (1:46)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Estimated TST at night, hour:min</td>
<td>8:17 (1:20)</td>
<td>8:55 (1:49)</td>
<td>0.002</td>
</tr>
<tr>
<td>Night sleep latency, min</td>
<td>11.06 (14.95)</td>
<td>21.41 (41.25)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Number of awakenings per night</td>
<td>1.18 (2.00)</td>
<td>1.85 (3.11)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Presence of daytime napping, yes (n, %)</td>
<td>31 (40.26 %)</td>
<td>33 (42.86 %)</td>
<td>0.59</td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>--------</td>
</tr>
<tr>
<td>TST over 24h, hour:min</td>
<td>8:42 (1:49)</td>
<td>9:20 (2:14)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Sleep habits - Weekends</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed time, hour:min</td>
<td>23:22 (1:07)</td>
<td>23:45 (1:29)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Wake-up time, hour:min</td>
<td>9:04 (1:31)</td>
<td>9:37 (1:50)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time spent in bed, hour:min</td>
<td>9:42 (1:39)</td>
<td>9:52 (1:39)</td>
<td>0.28</td>
</tr>
<tr>
<td>Estimated TST at night, hour:min</td>
<td>9:28 (1:36)</td>
<td>9:36 (1:39)</td>
<td>0.41</td>
</tr>
<tr>
<td>Night sleep latency, min</td>
<td>9.85 (13.46)</td>
<td>20.16 (41.47)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of awakenings per night</td>
<td>1.14 (2.05)</td>
<td>1.85 (3.02)</td>
<td>0.002</td>
</tr>
<tr>
<td>Presence of daytime napping, yes (n, %)</td>
<td>40 (51.95 %)</td>
<td>38 (49.35 %)</td>
<td>0.56</td>
</tr>
<tr>
<td>TST over 24h, hour:min</td>
<td>10:07 (2:05)</td>
<td>10:11 (2:12)</td>
<td>0.57</td>
</tr>
<tr>
<td><strong>Sleep habits - Weekdays vs Weekends</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DELTA DIFF bedtime, min</td>
<td>38.80 (44.94)</td>
<td>25.60 (45.46)</td>
<td>0.004</td>
</tr>
<tr>
<td>DELTA DIFF wake-up time, min</td>
<td>110.40 (102.06)</td>
<td>67.93 (90.72)</td>
<td>0.0004</td>
</tr>
<tr>
<td>DELTA DIFF Time spent in bed, min</td>
<td>71.60 (92.78)</td>
<td>42.33 (75.63)</td>
<td>0.01</td>
</tr>
<tr>
<td>DELTA DIFF Estimated TST at night, min</td>
<td>70.44 (71.59)</td>
<td>41.40 (68.42)</td>
<td>0.001</td>
</tr>
<tr>
<td>DELTA DIFF Estimated TST over 24h, min</td>
<td>85.04 (88.12)</td>
<td>51.69 (83.61)</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Self-questionnaires</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epworth sleepiness scale total score</td>
<td>12.41 (5.37)</td>
<td>12.49 (5.34)</td>
<td>0.62</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>68.85 (20.26)</td>
<td>66.83 (20.38)</td>
<td>0.07</td>
</tr>
<tr>
<td>Idiopathic Hypersomnia Severity Scale total score</td>
<td>28.13 (10.86)</td>
<td>28.48 (11.26)</td>
<td>0.96</td>
</tr>
</tbody>
</table>

**Abbreviations:** DELTA DIFF = Delta of the difference, EQ-5D = European Quality of life five-dimensions questionnaire, TST = total sleep time, VAS = visual analog scale. Continuous variables are expressed as numbers; means (± standard deviation)
TABLE 3. Comparison of sleep habits and self-questionnaires before and during lockdown in patients with restless legs syndrome.

<table>
<thead>
<tr>
<th>PATIENTS WITH RESTLESS LEGS SYNDROME</th>
<th>N=148</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before lockdown</td>
</tr>
<tr>
<td><strong>Sleep habits - Weekdays</strong></td>
<td></td>
</tr>
<tr>
<td>Bed time, hour:min</td>
<td>23:05 (0:58)</td>
</tr>
<tr>
<td>Wake-up time, hour:min</td>
<td>06:56 (1:19)</td>
</tr>
<tr>
<td>Time spent in bed, hour:min</td>
<td>7:51 (1:20)</td>
</tr>
<tr>
<td>Estimated TST at night, hour:min</td>
<td>6:26 (1:32)</td>
</tr>
<tr>
<td>Night sleep latency, min</td>
<td>29.27 (24.75)</td>
</tr>
<tr>
<td>Number of awakenings per night</td>
<td>2.50 (2.39)</td>
</tr>
<tr>
<td>Presence of daytime napping, yes (n, %)</td>
<td>56 (40.88 %)</td>
</tr>
<tr>
<td>TST over 24h, hour:min</td>
<td>6:44 (1:39)</td>
</tr>
<tr>
<td><strong>Sleep habits - Weekends</strong></td>
<td></td>
</tr>
<tr>
<td>Bed time, hour:min</td>
<td>23:17 (0:59)</td>
</tr>
<tr>
<td>Wake-up time, hour:min</td>
<td>07:30 (1:32)</td>
</tr>
<tr>
<td>Time spent in bed, hour:min</td>
<td>8:14 (1:27)</td>
</tr>
<tr>
<td>Estimated TST at night, hour:min</td>
<td>6:42 (1:42)</td>
</tr>
<tr>
<td>Night sleep latency, min</td>
<td>28.43 (23.92)</td>
</tr>
<tr>
<td>Number of awakenings per night</td>
<td>2.51 (2.41)</td>
</tr>
<tr>
<td>Presence of daytime napping, yes (n, %)</td>
<td>66 (48.18 %)</td>
</tr>
<tr>
<td>TST over 24h, hour:min</td>
<td>7:01:54 (1:45:40)</td>
</tr>
<tr>
<td></td>
<td>DELTA DIFF bedtime, min</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td>12.11 (28.30)</td>
</tr>
<tr>
<td></td>
<td>34.05 (55.78)</td>
</tr>
<tr>
<td>Self-questionnaires</td>
<td></td>
</tr>
<tr>
<td>Epworth sleepiness scale total score</td>
<td>8.54 (5.66)</td>
</tr>
<tr>
<td>Insomnia Severity Index total score</td>
<td>13.43 (5.86)</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>68.09 (17.39)</td>
</tr>
<tr>
<td>IRLS total score</td>
<td>19.83 (7.69)</td>
</tr>
</tbody>
</table>

**Abbreviations:** DELTA DIFF = Delta of the difference, EQ-5D = European Quality of life five-dimensions questionnaire, IRLS = International Restless Legs Syndrome Study Group questionnaire, TST = total sleep time, VAS = visual analog scale.
Continuous variables are expressed as numbers; means (± standard deviation)
Changes in Sleep Pattern During the COVID-19 Lockdown in Patients With Narcolepsy, Idiopathic Hypersomnia, and Restless Legs Syndrome
Lucie Barateau, Sofiene Chenini, Anna Laura Rassu, et al.

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