JCSM Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Adjustment to lockdown in children and adolescents with narcolepsy in France

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Study Objectives: The goal of the current study was to explore the effect of a 2-month quarantine on children and adolescents with narcolepsy and to describe the changes in their sleep, mood, and metabolism during this period.

Methods: The study involved 77 patients aged 7 to 23 years with a diagnosis of narcolepsy. Participants had to answer multiple-choice questions to characterize the changes and modifications in their own habits and state of health.

Results: Participants reported changes in daytime sleep, nighttime sleep schedules, treatment intake, food intake, weight, and amount of screen time. Most patients reported deterioration in their memory and attention abilities as well as a decrease in their work efficiency. Mood appeared to be less affected, although it deteriorated in less than one-third of the participants who reported feeling sad more often.

Conclusions: The prolonged and complete lockdown seemed to have an effect on children and adolescents with narcolepsy, and changes are often considered by the participants to depend on or to determine an overall quality of adaptation to the situation. This study highlights the importance of maintaining and strengthening time markers in individuals with narcolepsy and should help to establish guidelines that would apply in future quarantine situations. **Keywords:** narcolepsy, lockdown, sleep, child, time markers, adaptation

Citation: de Laclause AP, Konofal E, Bokov P, Delclaux C, Lecendreux M. Adjustment to lockdown in children and adolescents with narcolepsy in France. J Clin Sleep Med. 2022;18(9):2247–2252.

BRIEF SUMMARY

Current Knowledge/Study Rationale: The effect of prolonged lockdown due to the COVID-19 pandemic on chronic diseases such as narcolepsy is unknown. Such an atypical period could lead to changes in zeitgebers, mood, or cognitive performance.

Study Impact: This study highlights the importance of maintaining and strengthening time markers such as stable sleeping and eating schedules in individuals with narcolepsy, as well as the importance of clinicians encouraging treatment uptake and scheduling. The study should help to establish guidelines that would apply in any future situations of strict lockdown to avoid aggravation of symptoms, particularly concerning mood and emotion regulation, and to avoid accentuating comorbidities such as mood disorders or weight gain.

INTRODUCTION

The effect of prolonged lockdown due to the COVID-19 pandemic on chronic diseases such as narcolepsy is unknown.

Narcolepsy is a rare central hypersomnia that affects 20 to 60 people of 100,000 worldwide.^{1,2} It is a chronic condition characterized by irresistible sleep attacks during the day, abnormalities in sleep structure, excessive daytime sleepiness, and in most cases cataplexy, which is defined by a loss of muscle tone that can lead to falling, mainly triggered by emotions.³ Current diagnostic criteria specified in the *International Classification of Sleep Disorders*, third edition distinguishes 2 forms of the disease: patients with type 1 narcolepsy have a loss of the neuropeptide hypocretine-1/orexin-A in the cerebrospinal fluid and are prone to cataplexy attacks, whereas the level of hypocretine-1/orexin-A is normal and cataplexy attacks are absent in type 2 narcolepsy.

Narcolepsy is a life-long condition that often begins during $childhood^4$ and requires specific management and constant

adjustments to facilitate not only school rhythm and academic performance but also quality of life. The dramatic and abrupt change of life conditions dictated by the complete and prolonged lockdown enacted by the French authorities from March to May 2020 for sanitary reasons led to a major change in the habits of the French pediatric population, including those who presented with a chronic condition such as narcolepsy.

During lockdown, the schedules for hygiene care, meals, bedtime, and wake-up may be shifted or disordered and the function of time markers is lost. Set up under the influence of zeitgebers, the circadian process remains sensitive to changes in lifestyle habits. By processing signals from lifestyle habits, the biological clock can anticipate the body's needs and respond in time using hormonal messengers such as melatonin from the suprachiasmatic nucleus of the hypothalamus. Thus, a disturbance of the internal clock causes a disruption of the sleep/ wake cycle, body temperature, metabolism, and food intake,^{5,6} particularly impaired in patients with narcolepsy.

Some authors suggested that children with narcolepsy are exposed to emotional regulation difficulties⁷ that could be challenged by unexpected situations such as the lockdown, resulting in mood deterioration and increased anxiety. Attention issues are also estimated to be twice as common in children with narcolepsy as in the general pediatric population⁸ and may also be modified by stressful environmental conditions. Increase of inattention as well as sleep disturbance leads to poor academic and school performance in the general pediatric population.^{9,10}

From March to May 2020, the French population faced an unprecedented quarantine situation due to the rapid progression of COVID-19 in Europe, which included closure of schools for approximately 2 months.¹¹

Children were asked to stay home, where they received online instruction and took courses delivered by their own teachers according to the regular school schedules.

Some consequences of the lockdown could be significant factors influencing narcolepsy symptoms and associated difficulties.

Therefore, this study is aimed to determine the effect of a prolonged lockdown on narcolepsy core symptoms such as sleep and cataplexy but also metabolic features such as weight regulation and food intake, emotional aspects including mood and anxiety, and cognitive function in children and adolescents with narcolepsy.

METHODS

Data collection and population

An online auto-questionnaire adapted for children and adolescents was submitted to the patients with narcolepsy seen during the lockdown period at the Pediatric Centre for Sleep Disorders and National Reference Centre for Narcolepsy at Robert-Debré Hospital in Paris.

During the second half of April 2020, participants were asked to answer multiple-choice questions based on clinical expertise to characterize the changes and modifications in their own state of health during lockdown. A survey was developed by a group of sleep experts at the Reference Center of Sleep Diseases and Rare Hypersomnias at Robert-Debré Hospital. Participants answered the questionnaire only once, and any potential modifications were reflected in the questions and multiple-choice answers (for example: Since the beginning of lockdown, nap length 1) increased 2) decreased 3) stayed the same). The questionnaire was based on daytime and nighttime sleep schedules, napping habits, frequency of cataplexy, treatment intake, food intake during and between meals, feelings of sadness or anxiety, memory, attention, perceived work efficiency, and overall adaptation to the situation. All questions were answered 6 weeks after the beginning of the lockdown, before its end. The answers were based on participants' estimation of the changes that occurred since the beginning of the lockdown.

All the patients involved in the study had a diagnosis of narcolepsy type 1 according to international criteria (American Academy of Sleep Medicine, 2014).

All participants were HLA DQB1*06:02 positive and exhibited a low hypocretin level, \leq 110 pg/mL (80% underwent a

lumbar puncture), and/or presented with distinct cataplexy. Hypocretin-1 levels were determined from cerebrospinal fluid samples by direct radioimmunoassay (Phoenix Pharmaceuticals, Belmont, CA).

The study was approved by the local ethics committee of Robert-Debré Hospital.

Statistical analysis

Raw data were collected anonymously, and incomplete data were not processed. Statistical analyses were conducted with IBM SPSS Statistics 23.0 software.

All data were subject to descriptive statistics using frequencies and proportions.

Spearman correlations between proportions were established when relevant.

RESULTS

All the participants who received the questionnaire responded (n = 98). Of the 98 questionnaires received, 77 were suitable for analysis and 21 were incomplete. The final sample consisted of 77 participants, aged 7 to 23 years (mean = 15.16, standard deviation = 3.521) and with a diagnosis of narcolepsy. All patients met *International Classification of Sleep Disorders*, third edition clinical criteria for narcolepsy. Cataplexy attacks were experienced in 62 of 77 participants (80%, 95% confidence interval: 72–89%), and 21 of them (27%) reported sleep hallucinations (95% confidence interval: 17%–37%).

Wake-promoting agents were administered to 68 of 77 participants (88%, 95% confidence interval: 81–95%) and anticataplectic medication to 16 of 77 participants (21%, 95% confidence interval: 12–30%).

Descriptive statistics

Daytime sleep

The frequency of naps taken during lockdown was decreased for 8 of 77 participants (10%, 95% confidence interval: 3.5-17%), increased for 44 (57%, 95% confidence interval: 22-43%) and remained unchanged for 25 (32%, 95% confidence interval: 46–68%).

The duration of naps was decreased in 6 cases (8%, 95% confidence interval: 2–14%), unchanged in 35 (45%, 95% confidence interval: 34–56%), and increased in 36 (47%, 95% confidence interval: 35–58%).

Naps ranged from zero (no nap) to 240 minutes with an average time of 61 minutes.

Napping schedules were modified in 50 participants (65%, 95% confidence interval: 54–76%).

Of the 77 participants, sleep attacks were more frequent in 22 (29%, 95% confidence interval: 18–39%), less frequent in 28 (36%, 95% confidence interval: 25–47%), and of equivalent frequency in 27 (35%, 95% confidence interval: 24–46%).

The frequency of sleep attacks is shown in **Table 1**.

	Number	Percentage
Never	13	16.9
More than once a week	24	31.2
Once a day	26	33.8
More than once a day	14	18.2

Nighttime sleep

Bedtime was delayed by 1 hour or more in 59 of 77 participants (77%, 95% confidence interval: 67–86%).

The frequency of nightmares remained unchanged for 48 participants (62%, 95% confidence interval: 51-73%), increased for 23 (30%, 95% confidence interval: 20-40%), and decreased for 6 (8%, 95% confidence interval: 2-14%).

The frequency of nocturnal awakenings remained unchanged for 28 participants (36%, 95% confidence interval: 25-47%), decreased for 25 (32%, 95% confidence interval: 22-43%), and increased for 24 (31%, 95% confidence interval: 21-42%).

Total 24-hour sleep time increased in 41 of 77 participants (53%, 95% confidence interval: 42–64%), decreased for 15 (19%, 95% confidence interval: 11–28%), and remained unchanged for 21 (27%, 95% confidence interval: 17–37%). Total sleep time ranged from 4 to 24 hours a day, with an average of 10 hours and 50 minutes.

Sleep quality during lockdown was self-estimated from "very satisfied" to "very dissatisfied" as shown in Table 2.

Severity of self-reported intrasleep awakenings was also estimated by the participants as shown in **Table 3**.

Cataplexy

During lockdown, the frequency of cataplexy, including partial and generalized, triggered or spontaneous, decreased in 22 of the 65 participants experiencing cataplexy attacks (36%, 95% confidence interval: 23–47%), increased for 15 of 65 participants (24%, 95% confidence interval: 13–35%), and remained unchanged for 25 of 65 participants (40%, 95% confidence interval: 28–53%).

The frequency of cataplexy is shown in **Table 4**.

Weight and food intake

Of the 77 study participants, weight increased in 36 (47%, 95% confidence interval: 36–58%), weight decreased in 10 (13%,

Table	2—Self-estimated	quality	of	sleep.
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	Number	Percentage
Very dissatisfied	10	13.0
Rather dissatisfied	16	20.8
Moderately satisfied	29	37.7
Rather satisfied	15	19.5
Very satisfied	7	9.1

Table 3—Severity of intrasleep awakenings.

	Number	Percentage
No severity	20	26.0
Slight severity	23	29.9
Moderate severity	23	29.9
High severity	8	10.4
Extreme severity	3	3.9

95% confidence interval: 5–20%), and weight remained stable in 31 (40%, 95% confidence interval: 29–51%).

The amount of food taken at meals was increased in 31 cases (40%, 95% confidence interval: 29–51%), decreased in 13 cases (17%, 95% confidence interval: 8–25%), and remained unchanged in cases (43%, 95% confidence interval: 32–54%).

Forty-seven of the 77 participants (61%) were snackers (95% confidence interval: 50–72%). Of these, 26 (55%) were daytime snackers (95% confidence interval: 41–70%), 9 (19%) were nighttime snackers (95% confidence interval: 8–30%), and 12 (25%) were day and night snackers (95% confidence interval: 13–38%).

During quarantine, of the 47 participants the frequency of snacking increased in 29 (62%, 95% confidence interval: 47–76%), decreased in 4 (8%, 95% confidence interval: zero to 23%), and remained unchanged in 14 (30%, 95% confidence interval: 15–44%).

Cognitive effects

Of the 77 participants, academic efficiency decreased during quarantine in 47 (61%, 95% confidence interval: 50–72%), was more efficient in 12 (16%, 95% confidence interval: 4–27%), and no difference was noted in 18 (23%, 95% confidence interval: 12-35%).

Thirty-seven participants (48%) observed a deterioration in memory and attention span (95% confidence interval: 37–59%), 10 (13%) observed an improvement (95% confidence interval: 2–24%), and 30 (39%) reported no change (95% confidence interval: 28–50%).

Mood and adaptation

During lockdown, of 77 participants, 17 (22%) felt sad more often (95% confidence interval: 11-33%), 12 (16%) felt sad less often (95% confidence interval: 4-27%), and 48 (62%) noted no change (62%, 95% confidence interval: 51-73%) of cases.

	Table	4 —F	requency	of	cataplexies	
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	Number	Percentage
Less than once a week	23	37.1
One to six a week	16	25.8
Once a day	12	19.4
More than once a day	11	17.7

Table 5—Participants' self-estimated adaptation.

	Number	Percentage
Good	9	11.7
Rather good	32	41.6
Rather bad	32	41.6
Bad	4	5.2

Of the 77 participants, 25 (32%) felt more anxious (95% confidence interval: 21–44%), 14 (18%) felt less anxious (95% confidence interval: 7–29%)

Participants' self-reported level of adaptation is shown in Table 5.

Screen time consumption

Most of the participants (69 of 77 [90%], 95% confidence interval: 78–100%) increased their screen time consumption during lockdown.

Treatment

Among the 68 patients treated with wake-promoting agents (methylphenidate, modafinil, or pitolisant), 25 (37%) modified the daily dose (95% confidence interval: 25%–49%). The treatment was changed by the patient in 22 cases (88%, 95% confidence interval: 68%–100%) and by the physician in charge of the patient in only 3 cases (12%, 95% confidence interval: zero to 32%). The dose was increased in only 3 of these 68 patients (4%, 95% confidence interval: zero to 16%) and spontaneously decreased in the remaining 65 cases (96%, 95% confidence interval: 84–100%).

Among the patients undergoing anticataplectic treatment, the dose was spontaneously decreased in 2 of 16 (13%, 95% confidence interval: 0 to 37%), and once on medical advice.

Significant correlations

In view of the significant correlations found between variables, some similarities can be hypothesized regarding the different repercussions of lockdown on children and adolescents with narcolepsy.

Thus, work efficiency is positively correlated with quality of sleep (r = .281, P < .05) and perceived adaptation to lockdown (r = .340, P < .05).

Negative correlations were found between work efficiency and increase in screen time (r = -.336, P < .05), increase in the frequency of naps (r = -.293, P < .05), and deteriorations in memory and concentration (r = -.366, P < .05).

Among the mood changes reported, feelings of sadness were correlated with increased frequency of napping (r = .283, P < .05), weight gain (r = .283, P < .05), anxiety (r = .514, P < .05), and perceived adaptation to lockdown (r = -.278, P < .05).

Anxiety is itself correlated with decrease in treatment dosage (r = .254, P < .05).

The self-estimated degree of adaptation to the situation, characterized by the participants themselves, appears to be correlated with a number of criteria such as the frequency of naps (r=-.335, P < .05), the duration of naps (r=-.252, P < .05), changes in food intake (r=-.228, P < .05), self-estimated work efficiency (r=.340, P < .05), and sadness (r=-.278, P < .05).

DISCUSSION

The objective of this study was to describe the changes experienced by children and adolescents with narcolepsy in the manifestation of the disease, sleep, food intake, mood, and work efficiency during lockdown from March to May 2020.

Participants reported changes about daytime sleep, nighttime sleep schedules, food intake, screen time consumption.

Daytime and nighttime sleep

The frequency and duration of naps were often increased, sometimes unchanged, and rarely decreased. Bedtime was delayed by 1 hour or more in most cases, and the total sleep time for 24 hours was more important than usual.

Consistent with these findings, an increase in bedtime hours, bedtime delay, and daytime napping was found in students and adults with type 1 narcolepsy working from home during COVID lockdown.¹² Similar changes were observed in students and adults working from home without narcolepsy.¹³

Filardi et al¹⁴ found a delayed sleep phase and an increase in daytime sleep during lockdown in pediatric patients with type 1 narcolepsy in Italy.

Weight and food intake

Weight gain was seen in most patients. Most participants reported consuming food between meals during lockdown. An increase in food intake was also observed by Postiglione et al¹² during lockdown in adult patients with type 1 narcolepsy.

Screen consumption, cognitive aspects, mood, and anxiety

Most patients also increased the time spent in front of screens during lockdown.

Quaedackers et al¹⁵ also reported findings concerning a pediatric population with narcolepsy. In 2 of 3 cases, the lockdown had positive effects, such as mood improvement and better work efficiency.

Conversely, most of the current study participants reported deterioration in memory and attention abilities as well as a decrease in self-reported work efficiency based on self-estimation.

Mood appeared to be less affected, although deteriorated in less than one-third of the participants who reported feeling sad more often. One-fifth of the participants described themselves as sad less often, and the rest of the participants reported no change in mood. Anxiety decreased during lockdown for nearly one-fourth of the participants, increased for more than one-third, but remained unchanged for most participants. Depressive mood and anxiety were also found in adults with narcolepsy during lockdown in Italy.¹⁶

These findings were also found in the general pediatric population. A meta-analysis by Panda et al¹⁷ reported an increase in screen consumption, cognitive difficulties, and mood degradation such as sadness and anxiety. Orgilés et al¹⁸ reported more difficulty concentrating (76.6% of their participants) and a lower increase in sleep duration (22 minutes) than in the current study.

The results of the current suggest a relationship between sleep quality and scholar efficiency, such that an increase in sleep quality would lead to better productivity. An association between sleep disturbances and school and academic performance had indeed been demonstrated earlier in the general population.^{9,10}

However, work efficiency seemed to decrease when screen time or napping frequency increased. Thus, more participants who reported a decrease in work efficiency increased the frequency and duration of their naps than in the overall sample.

Similarly, participants often reported both decreased academic performance and deterioration in attention and memory. However, these changes do not appear to affect mood and anxiety. Sadness was associated with frequent naps, increased weight, and anxiety, whereas increased anxiety was associated with decreased treatment dosage during lockdown.

Last, an adaptation estimated by participants as "good" to "very good" could depend on a decrease in the frequency and duration of naps, food intake, and sadness and improved work productivity.

Effect of changes in zeitgebers

In this study, the change of rhythm and loss of zeitgebers (school, meals, and bedtime schedules) resulted in behavioral changes in most patients who tended to sleep more, change their nap times, and shift their night sleep, take less medication, and increase their weight.

A positive effect seems to be observed for a smaller proportion, but this was not the case for most of the participants, who showed adaptation difficulties. The results of this study are consistent with the recommendations in a rare pathology of sleep and wakefulness regulation, where it is important to maintain some regular time markers.

This study presents a good response rate of 70%.

Limitations and perspectives

The limitations could be the small sample of participants that led to a lack of statistical power, the particular structure of the questionnaire and type of questions that did not enable the use of inferential statistics, and the lack of a prelockdown baseline.

This study lacks standardized measures because of the absence of such tools in the field of pediatric narcolepsy and lockdown.

Furthermore, there is no baseline or historical data for comparison.

A future study should consider the results from this study and similar studies conducted during the COVID-19 lockdown.

In a future study, it seems important to determine the emotional profile (depression and anxiety) of the participants and its role in the adaptation of children with narcolepsy to such a situation of isolation at home and a decrease in social time markers, because sleep, mood, and anxiety appear to be strongly linked in almost one-third of the participants. These at-risk participants should be followed up carefully by the clinicians and investigated with standardized questionnaires. It is likely that some children increase their sleep duration (number of naps) in response to a mood alteration, when others take advantage of the possibility of free-napping schedules for better school performance and improved well-being independent of pharmacologic treatment. Reducing the amount of medication seems to increase anxiety in some children, which should encourage the clinician to closely manage patients during lockdown periods.

CONCLUSIONS

This study is one of few to describe the changes encountered in a pediatric population with narcolepsy during prolonged lockdown. For most participants, these changes concern day and night sleep, food intake and weight, treatment intake, time spent in front of screens, mood, and work efficiency. These changes are often considered by the participants to depend on or determine an overall quality of adaptation to the situation. The cognitive and emotional drivers of this adaptation to lockdown should be further investigated, and some dimensions appear to be important to monitor in case of lockdown, and even more generally, in children and adolescents with narcolepsy. Sleep, eating, and screen practice habits could be taken into account during follow-up because they seem to influence mood, anxiety, and productivity.

This study highlights the importance of maintaining and strengthening time markers in the patient population with narcolepsy, such as stable sleeping and eating schedules, as well as the importance of clinicians to encourage treatment uptake and scheduling.

The study should help to establish guidelines that would apply in the eventual future situations of more or less strict lockdown to avoid aggravation of symptoms, particularly concerning mood and emotion regulation, and to avoid accentuating comorbidities such as mood disorders or weight gain.

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ACKNOWLEDGMENTS

The authors thank the members of the French Association Nationale de Narcolepsie Cataplexie et d'hypersomnies rares and their families for their collaboration on the study.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication June 24, 2021 Submitted in final revised form April 27, 2022 Accepted for publication April 27, 2022

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DISCLOSURE STATEMENT

All authors have seen and approved this manuscript. Work for this study was performed at National Reference Center for Narcolepsy and Rare Hypersonnias, Hospital Robert-Debré, Paris, France. The authors report no conflicts of interest.