Effect of lockdown during COVID-19 on migraine: a longitudinal cohort study

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Abstract

Background: The objective of this study was to assess whether migraine-related outcomes changed during intelligent lockdown when compared with the prior period.

Methods: This was a cohort study evaluating the first month of intelligent lockdown in the Netherlands (12 March to 8 April 2020) compared with one baseline month (13 February to 11 March 2020). We identified 870 migraine patients treated at the Leiden Headache Center with headache e-diaries during the period of interest. Adherence to the e-diary had to be $\geq$80%, yielding 592 enrolled patients.

Results: Intelligent lockdown led to a decrease in monthly migraine days (-0.48; 95% CI: -0.78 to -0.18, $p = 0.002$) and acute medication days (-0.48; 95% CI: -0.76 to -0.20, $p < 0.001$), and an increase in general well-being (0.11; 95% CI: 0.06 to 0.17, $p < 0.001$). No differences in non-migrainous headache days and pain coping were observed. Consistent results were found in a subset that was followed for 4 months.

Conclusions: Our findings imply that intelligent lockdown measures can improve migraine disability despite of the potential negative effects of COVID-19 and lockdown. We hypothesise that this effect is a combined result of working from home, scaling down demanding social lives, and freedom to choose how to organise one's time.

Keywords

Headache, lifestyle changes, triggers, e-diary, telemedicine

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Introduction

The recent coronavirus (COVID-19) outbreak has an enormous global impact, both on individual and societal level. Worldwide healthcare systems have sought ways to adapt to the "new normal". Consequently, telemedicine has become an effective and feasible way to ascertain continuation of patient care (1–3). For paroxysmal neurological disorders such as migraine, e-diaries are a useful tool as they help gain insight into attack frequency and treatment response (4). We have recently developed a headache e-diary, which puts us in the unique position to look into the effects of the current lockdown on an individual level in migraine patients.

Migraine attacks are considered to be the result of natural fluctuations in neuronal excitability and trigger factors (5,6). Trigger factors are thought to contribute to precipitating an attack when natural excitability peaks. These trigger factors (e.g. stress, sleep), but also ways to handle attacks, could be affected by lockdown measures. In the Netherlands an "intelligent lockdown" was adopted starting on 12 March 2020, during which gatherings were banned and only limited outdoor activities with 1.5m (5ft) social distance were allowed. On 15 March schools, sport clubs, restaurants, and businesses dependent on physical contact were closed.

The aim of this study was to assess whether lockdown measures influence migraine-related outcomes.

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Methods

For this cohort study we identified patients diagnosed with migraine (3,7) and treated at the Leiden Headache Center for whom headache e-diaries were available during 28 baseline days (13 February to 11 March) and the first 28 days of lockdown (12 March to 8 April). In addition, a subset was selected for whom e-diaries were available during one additional baseline month (16 January to 12 February) and one additional lockdown month (9 April to 6 May). Patients had to adhere to the e-diary for at least 80% per 28 day period. This study was approved by the medical ethics committee of the Leiden University Medical Center (LUMC).

Patients received a daily time-locked e-diary with questions attributing headache presence, characteristics, and associated symptoms, use of acute pain medication, change in prophylactic headache medication, well-being, and pain coping. An automatic algorithm calculates for each day whether it is a headache day. A headache day is defined as a day with a headache lasting for at least 1 h and/or use of any acute treatment (analgesics or triptans). If a headache is present, the algorithm verifies diagnostic criteria for migraine according to the International Classification of Headache Disorders (ICHD-3) (8) and/or triptan intake. Headache days not fulfilling these criteria are labelled as non-migrainous headache days. Patients rate their pain coping ability and general well-being on a continuous scale from 1 (worst) to 10 (best). Pain coping is rated on all headache days and general well-being on each day.

We primarily examined the change in number of monthly migraine days between 1 month (28 days) baseline and 1 month (28 days) lockdown. Secondary outcome variables were change in monthly acute medication days, non-migrainous headache days, general well-being and pain coping. In addition, change between 2 months (56 days) baseline and 2 months (56 days) lockdown were examined in a subset of patients with more data available. Age, sex, lifetime depression, diagnosis of chronic migraine, and changes in prophylactics were considered potential confounders. Lifetime depression was defined as a HADS-D $\geq$8 or CES-D $\geq$16 or (past) depression diagnosed by a physician or (past) use of antidepressants for depression (9). Chronic migraine was defined as $\geq$15 headache days/month, from which $\geq$8 were migraine days

Table 1. Baseline characteristics of included migraine patients.

	Total cohort (2 months follow-up)	Subset (4 months follow-up)
Number of patients	592	469
Age, mean (SD), years	46.2 (12.2)	47.0 (12.3)
Female sex, n (%)	483 (81.6%)	373 (79.5%)
Diagnosis		
Migraine with aura, n (%)	141 (23.8%)	114 (24.3%)
Migraine without aura, n (%)	370 (62.5%)	287 (61.2%)
Chronic migraine, n (%)	81 (13.7%)	68 (14.5%)
Lifetime depression, n (%)	283 (47.8%)	229 (48.8%)
Change in prophylactic therapy, n (%)	83 (14.0%)	68 (14.5%)

Note: Chronic migraine was defined as $\geq$15 headache days/month, from which $\geq$8 were migraine days. Lifetime depression was defined as a HADS-D $\geq$8 or CES-D $\geq$16 or (past) depression diagnosed by a physician or (past) use of antidepressants for depression. Change in prophylactic therapy was defined as starting, dosage change or stopping prophylactics during the study period.

Table 2. Migraine-related outcomes during 28 days baseline and 28 days lockdown (n = 592 migraine patients).

Mean (SD)	Baseline (28 days)	Lockdown (28 days)	Crude mean difference (95% CI)	Adjusted mean difference (95% CI)	*p*-value
Diary compliance	27.22 (1.38)	27.17 (1.48)			
Migraine days	7.39 (5.94)	6.92 (5.78)	−0.47 (−0.77, −0.18)	−0.48 (−0.78, −0.18)	0.002
Non-migrainous headache days	4.72 (5.87)	4.48 (5.82)	−0.24 (−0.49, −0.01)	−0.25 (−0.50, 0.002)	0.05
Acute medication days	5.47 (4.90)	4.99 (4.55)	−0.48 (−0.77, −0.21)	−0.48 (−0.76, −0.20)	<0.001
Well-being	6.35 (1.68)	6.47 (1.67)	0.11 (0.06, 0.17)	0.11 (0.06, 0.17)	<0.001
Pain coping	5.33 (1.53)	5.41 (1.57)	0.07 (0.003, 0.14)	0.07 (−0.001, 0.15)	0.05

Note: Well-being and pain coping were daily rated on a continuous scale from 1 (worst) to 10 (best). Pain coping was rated on all headache days and general well-being on each day. *p*-values were obtained from a linear mixed model, which was fitted for each variable of interest including potential confounders.

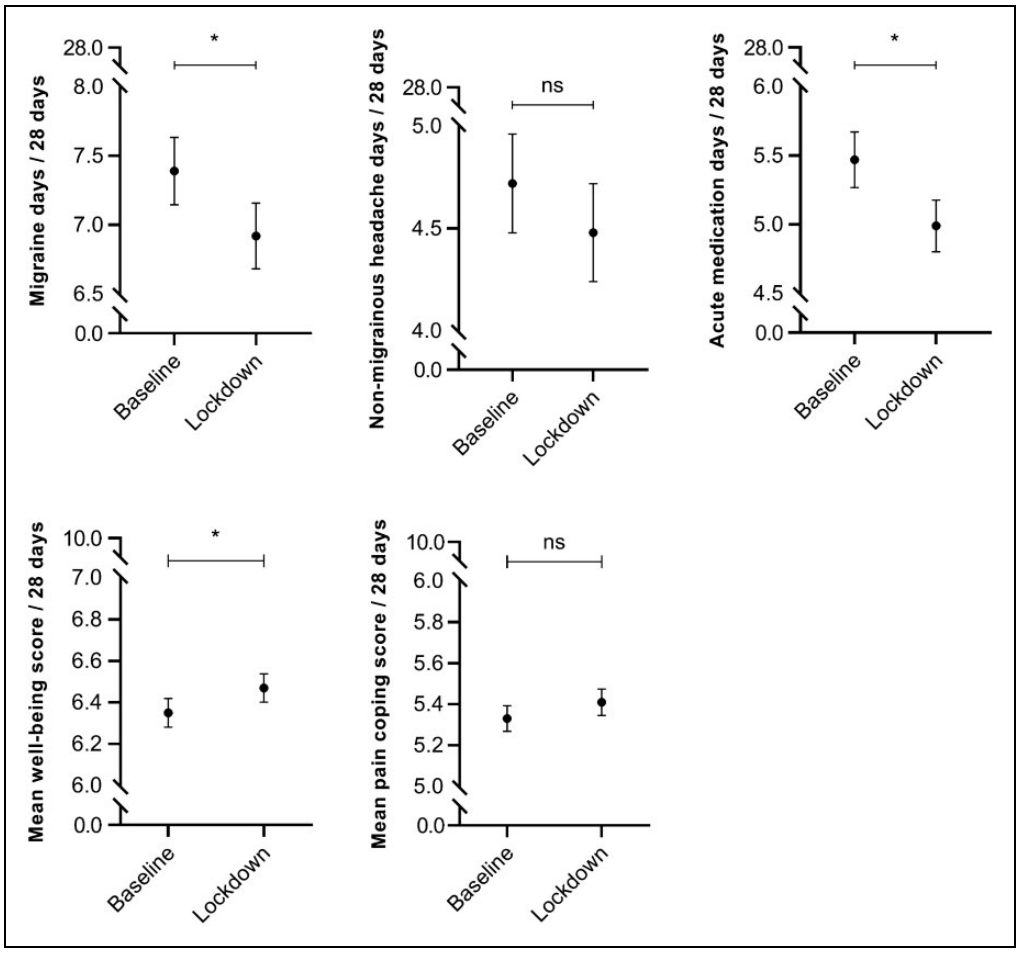

Figure 1. Crude means ± SEM for migraine-related outcomes during baseline (28 days) and lockdown (28 days) (n = 592 migraine patients). The presented *p*-values were obtained using a linear mixed model with correction for possible confounders.
*$p < 0.05$, ns: $p \geq 0.05$.

(8). Starting, dosage change or stopping prophylactics during the study were considered as change.

For each outcome variable, a linear mixed model was fitted for 28 days baseline versus 28 days lockdown and for 56 days baseline versus 56 days lockdown with age, sex, lifetime depression, chronic migraine and changes in prophylactic therapy as fixed effects and the patient as a random effect. Unstructured covariance matrices were used. Adjusted mean differences with 95% CI were reported, as well as crude unadjusted means with 95% CI. Two-sided *p*-values < 0.05 were considered statistically significant. All analyses were performed in R version 3.6.1.

Results

E-diary data from the period between 13 February 2020 and 8 April 2020 was available for 870 migraine patients, from which 278 were excluded as e-diary adherence was <80%/28 days, yielding 592 eligible migraine patients with 2 months follow-up. For 469 migraine patients, additional data was available from the period between 16 January and 6 May (4 months follow-up). The majority of included patients had migraine without aura. Approximately half of patients scored above the threshold on depression questionnaires or were diagnosed with a depression in the past. Around 15% of patients underwent a change in prophylactic treatment during the study period. Baseline characteristics of both the total cohort and subset are shown in Table 1.

After correction for possible confounders, we found a decrease in number of migraine days of −0.48 (95% CI: −0.78 to −0.18, $p = 0.002$) during the first month of lockdown when compared with one prior baseline month. In addition we found a decrease in acute medication days of −0.48 (95% CI: −0.76 to −0.20, $p < 0.001$) and an increase in general well-being of 0.11 (95% CI: 0.06 to 0.17, $p < 0.001$). We found no differences in number of non-migrainous headache

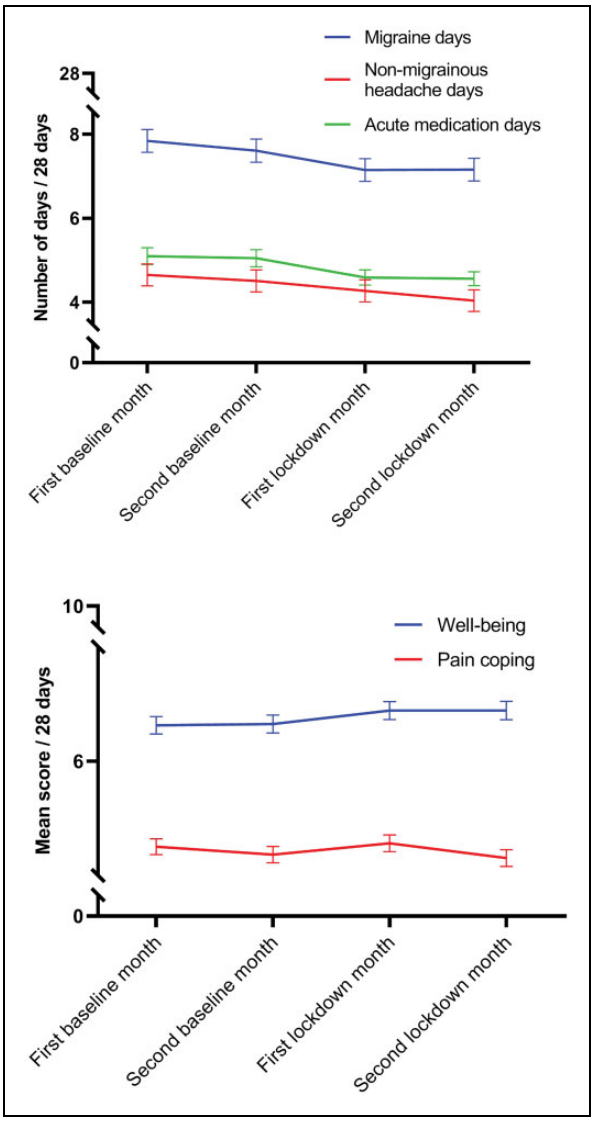

Figure 2. Course of migraine-related outcomes during 4 months of follow-up (n = 469 migraine patients). Presented are the crude means ± SEM. All months were a time period of 28 days.

days and pain coping. Crude estimates without statistical modelling and adjusted estimates are shown in Table 2 and Figure 1. We found consistent results in a subset of patients that was followed for 4 months. The course over 4 months is presented in Table 3 and Figure 2, whereas unadjusted and adjusted estimates are presented in Table 4.

Discussion

This longitudinal cohort study shows a decrease in number of migraine days, acute medication days and an increase in general well-being during lockdown when compared with the period prior to lockdown. Our findings imply that intelligent lockdown measures positively impact migraine specific outcome measures and general well-being. We hypothesise that this effect is a combined result of working from home, scaling down of demanding social lives and freedom to choose how to organise one's time. We speculate that, as a result, people have fewer work-related and social obligations and are able to take bed rest during a migraine attack, possibly decreasing the risk of recurrence. Naturally, many more contributing factors could be involved.

Our study has some major strengths. We developed a time-locked e-diary with an automated algorithm differentiating headache and migraine days based on detailed characteristics according to ICHD-3 criteria. The time-lock prevents patients from changing their input. All patients filling out e-diaries when lockdown was announced were eligible. Only diaries with sufficient data were included in our analyses in order to make reliable comparisons. We have performed a *post-hoc* sensitivity analysis including all patients with ≥60% adherence to the e-diary to make sure our findings were robust, which has led to consistent results (data not shown). Furthermore, we have found corresponding results in a subset of patients with prolonged

Table 3. Course of migraine-related outcomes during 4 months of follow-up (n = 469 migraine patients). All months were a time period of 28 days.

Mean (SD)	First baseline month	Second baseline month	First lockdown month	Second lockdown month
Diary compliance	27.45 (1.10)	27.34 (1.21)	27.28 (1.32)	27.28 (1.37)
Migraine days	7.84 (5.94)	7.61 (5.96)	7.15 (5.87)	7.16 (5.90)
Non-migrainous headache days	4.65 (5.68)	4.51 (5.72)	4.27 (5.64)	4.04 (5.60)
Acute medication days	5.10 (4.32)	5.05 (4.38)	4.59 (3.90)	4.56 (3.62)
Well-being	6.32 (1.70)	6.33 (1.73)	6.45 (1.72)	6.45 (1.76)
Pain coping	5.24 (1.53)	5.17 (1.56)	5.27 (1.60)	5.14 (1.62)

Note: Well-being and pain coping were daily rated on a continuous scale from 1 (worst) to 10 (best). Pain coping was rated on all headache days and general well-being on each day.

Table 4. Migraine-related outcomes during 56 days baseline and 56 days lockdown (n = 469 migraine patients).

Mean (SD)	Baseline (56 days)	Lockdown (56 days)	Crude mean difference (95% CI)	Adjusted mean difference (95% CI)	*p*-value
Diary compliance	27.40 (0.98)	27.28 (1.18)			
Migraine days	7.72 (5.68)	7.16 (5.63)	−0.57 (−0.87, −0.27)	−0.58 (−0.89, −0.28)	<0.001
Non-migrainous headache days	4.58 (5.48)	4.16 (5.45)	−0.42 (−0.67, −0.17)	−0.42 (−0.67, −0.17)	0.001
Acute medication days	5.07 (4.01)	4.57 (3.41)	−0.50 (−0.76, −0.23)	−0.50 (−0.77, −0.24)	<0.001
Well-being	6.32 (1.68)	6.45 (1.70)	0.13 (0.07, 0.19)	0.13 (0.07, 0.19)	<0.001
Pain coping	5.21 (1.49)	5.20 (1.55)	−0.001 (−0.07, 0.07)	−0.001 (−0.07, 0.07)	0.976

Note: Well-being and pain coping were daily rated on a continuous scale from 1 (worst) to 10 (best). Pain coping was rated on all headache days and general well-being on each day. *p*-values were obtained from a linear mixed model, which was fitted for each variable of interest including potential confounders.

follow-up duration. We feel this study is an excellent example of how e-diaries can be used for *ad-hoc* research and at the same time for telemedicine, as we were also able to continue our clinical follow-up by visualising e-diary data in the electronic patient records during video-consultation.

A limitation of this study is that lockdown came unexpectedly and therefore we could not assess the presence of each possible contributing factor. The lockdown has led to multiple changes, of which some will possibly decrease, and some will increase the susceptibility to a migraine attack. Lockdown may for instance increase stress, anxiety, and insecurity about health, (un)employment and financial situation, and homeschooling children can be an extra burden. In addition, closing of sport clubs and limited outdoor activities could induce weight gain. In the long term, these factors may also worsen migraine. After 2 months, on 11 May lockdown was lifted in the Netherlands. Long-term effects could therefore not be assessed. Despite these potentially harmful factors we were able to show an overall positive effect on migraine-related outcomes during 2 months of lockdown.

In addition, the run-up to actual implementation of lockdown or other measures might also be associated with insecurity and stress. This could potentially lead to a worsening of migraine disability prior to lockdown. In the Netherlands, there were only 2 weeks between the first COVID-19 diagnosis and establishment of the intelligent lockdown. In the analyses evaluating a longer follow-up period including 2 baseline months, we found no indication for a worsening of migraine-related outcomes shortly before lockdown when compared with the previous month.

This study was conducted in a tertiary headache center. Patients had a relatively high monthly attack frequency. Hence, the findings of this study may be restricted to more severely affected migraine patients. Due to our sample size, we chose not to perform sub-analyses on migraine subtypes and changes in prophylactic therapy. Despite the fact that regular care was given and treatment changes were made, we were still able to show an overall positive effect of lockdown, albeit the effect size seems small. Nonetheless, in more severely affected patients each reduction may have a significant impact on daily life activities and general well-being, as shown by our results.

In conclusion, our findings imply that intelligent lockdown measures can improve migraine disability. We hypothesise that this effect can be attributed to working from home and fewer social obligations, resulting in freedom to choose how to organise one's time to better reconcile suffering from migraine and work and social obligations. Under less stressful circumstances, these benefits may even be larger.

Clinical implications

- Migraine patients could benefit from lifestyle changes associated with intelligent lockdown, such as working from home, scaling down demanding social lives, and freedom to choose how to organise one's time.
- Headache e-diaries are a very useful telemedicine tool that can be used in clinical practice as well as for *ad-hoc* research.

Declaration of conflicting interests

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Supplementary data availability

Data on *post-hoc* sensitivity analyses and other data not published within the article will be shared by request from a qualified investigator.

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