Pain experience and mood disorders during the lockdown of the COVID-19 pandemic in the United States: an opportunistic study

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**ABSTRACT**

**Introduction:** The unknown and uncontrollable situation of the coronavirus disease 2019 (COVID-19) pandemic may have triggered changes in pain, anxiety, and depression along with a perception of nonspecific COVID-19 symptoms.

**Objectives:** We determined how anxiety, depression, and pain outcomes varied during the “Stay-at-Home” order compared with the prepandemic period and whether nonspecific COVID-19 symptoms would occur.

**Methods:** We conducted an online survey to opportunistically reassess clinical anxiety, depression, pain intensity, and pain interference while controlling for somatic symptom severity during the prepandemic and Stay-at-Home order period. During the Stay-at-Home period, anxiety, depression, pain intensity, and pain interference were reassessed. Coping strategies were assessed as a critical factor influencing pain behaviors. In addition, we explored the occurrence of nonspecific COVID-19 symptoms with an ad hoc survey referencing the Centers for Disease Control and Prevention publicly available COVID-19 symptoms.

**Results:** We observed a significant increase in depression and anxiety levels during the Stay-at-Home period. Coping strategy changes (eg, increased exercise) were linked to lower pain severity and interference which improved overall. Participants who self-reported nonspecific COVID-19 symptoms had higher prepandemic depression. Among the 72 participants not diagnosed with COVID-19, 70.8% of the participants experienced symptoms resembling those associated with COVID-19.

**Conclusion:** We suggest the parallel between pain outcome improvement and worsening anxiety and depression during the Stay-at-Home order might reflect a shift in symptoms, indicating that those patients with underlying mood disorders may require more help than they did before the pandemic.

**Keywords:** Mood disorder, Temporomandibular disorder, Expectations, Illness behaviors, Nocebo

1. **Introduction**

The pandemic of coronavirus disease 2019 (COVID-19)\textsuperscript{24,42} is one of the most serious outbreaks over the past century. It has induced significant distress and anxiety for patients\textsuperscript{55} and providers.\textsuperscript{7,62} Stress is the acute response to something fearful, unpredictable, and uncontrollable; it can also potentiate anxiety, an adaptive response that promotes harm avoidance.\textsuperscript{33} However, circumstances producing sustained distress, such as the COVID-19 pandemic, can result in overwhelming, excessive anxiety.\textsuperscript{31}

The symptomatology of COVID-19 has evolved from only flu-like symptoms to a variety of symptoms that have been continuously updated by the Centers for Disease Control and Prevention (CDC).\textsuperscript{21} The daily threat of being exposed to COVID-19 or, worse, infected, could trigger the occurrence of nonspecific symptoms mimicking mild COVID-19–related symptoms that are not actually caused by the virus.

The Stay-at-Home order in the United States, State of Maryland refers to the condition for which residents were required to stay at home except for necessary life supplies and medical reasons from March 30 to June 9, 2020. During this short window of time, we focused on this opportunistic study to determine how anxiety, depression, and pain outcomes change along with the occurrence of COVID-19 symptoms that we considered “nonspecific” symptoms given that they were reported by people who either tested negative or were not aware of having been infected.
in accordance with previous definitions. Based on the recent media coverage on COVID-19 and worldwide emotional and physiological distress, our research question was to determine how personality factors and pre-pandemic levels of anxiety and depression could have affected anxiety, depression, and pain outcomes during the stressful Stay-at-Home order. To further explore the role of psychosocial factors, we assessed chronic pain coping strategies before and during the Stay-at-Home order and anticipated that effective adjustments in lifestyle would have resulted in less severe pain and interference despite the higher levels of anxiety and depression. Based on these hypotheses, we propose a framework that describes a shift in illness behaviors (i.e., individual’s responses to their health status) as characterized by higher anxiety and depression and changes in pain and coping strategies to understand patients’ behaviors within the context of the self-isolation during the COVID-19 pandemic.

2. Methods and Materials

We conducted this opportunistic study in a cohort of patients with chronic pain and healthy controls with whom we had already conducted before the outbreak an in-person and in-depth assessment of pain intensity, pain interference, anxiety, and depression. The Stay-at-Home order in the United States and, namely, in the State of Maryland started March 30 and ended June 9. During this time, we received institutional review board approval, and from May 12 to June 1, 2020, we enrolled 74 participants who were required to self-isolate during the lockdown.

We restricted the time for conducting the study to a 21-day window of the Stay-at-Home order in the State of Maryland. Study participants included 57 adults suffering from chronic pain and 17 healthy participants (Demographics are presented in Table 1). The study was approved by the local Institutional Review Board Committee at the University of Maryland. Participants were already phenotyped before the pandemic (21.09 ± 11.77 months) at the University of Maryland Schools of Nursing and/or the Brotman Orofacial Clinic at the School of Dentistry (for the patients with chronic facial pain).

2.1. Survey tool and psychological questionnaires

Participants in this cohort were either healthy volunteers or patients who were diagnosed with temporomandibular disorder(s) pain (according to the Axis I Diagnostic Criteria for TMD [DC/TMD]) at the Brotman Facial Pain Clinic, School of Dentistry University of Maryland. The healthy volunteer group consisted of participants who did not use pain medication and did not have pain of any nature, neurological disorders, or psychiatric disorders.

In addition, patients with chronic pain had been evaluated in person to confirm the diagnosis of temporomandibular disorder (TMD), pain severity using the Graded Chronic Pain Scale (GCPS), and other overlapping chronic pain conditions (e.g., migraine, low back pain, irritable bowel syndrome, and fibromyalgia; also refer to Table 1).

2.1.1. Psychological tools

A 6-item online Health Insurance Portability and Accountability Act–compliant survey through Research Electronic Data Capture was used. The survey briefly inquired about being Act–compliant survey through Research Electronic Data Capture.

2.2. Statistics

2.2.1. Outcomes

Primary outcomes were pain intensity and pain interference assessed by GCPS. Secondary outcomes were anxiety assessed by STAI-II, depression assessed by BDI, and self-reported perception of COVID-19 symptomology. Explorative outcomes were somatic symptoms measured using the PHQ-15 and coping strategies assessed with the CPCI.

For the anxiety, depression, and chronic pain outcomes, we first conducted repeated-measures analysis of covariance (ANCOVA) to examine the changes in those primary and secondary outcomes during the prepandemic and Stay-at-Home order. The time (before vs after the pandemic) was treated as the within-subjects factor, and group (chronic pain vs healthy controls) was set as the between-subjects factor. The time range between the 2 time-point assessments was treated as covariate.

Next, we determined how prepandemic personality characteristics and fear of COVID-19 could have influenced anxiety and
depression during the Stay-at-Home order. To test this, separate hierarchical regressions were conducted with baseline anxiety and depression entered in block 1. Personality characteristics (neuroticism, extraversion, openness to experiences, agreeableness, and conscientiousness—prepandemic), fear of COVID-19 (during the pandemic), and group (chronic pain vs healthy participants) were treated as independent variables in block 2.

Within the chronic pain cohort, we tested how changes in pain coping strategies (delta scores of before and during the pandemic) were treated as independent variables in block 2 of each of the regression model. This part of analysis was limited to participants with chronic pain.

### 2.2.2. Coronavirus disease 2019 symptomatology

To determine how participants with chronic pain differed from healthy participants in the occurrence of nonspecific COVID-19 symptoms (yes or no), χ² tests were used to compare the proportion of participants who had COVID-19 nocebo-like symptoms. Moreover, to examine how anxiety and depression influenced the perception of nonspecific COVID-19 symptoms, repeated-measures ANCOVAs were conducted (1) to compare anxiety and depression between the participants who showed nonspecific COVID-19 symptoms and those who did not perceive symptoms and (2) to examine the changes of anxiety and depression before...
and during the Stay-at-Home order period. The 2 time points (before vs during the pandemic) were set as within-subjects factors. The perception of COVID-19 symptoms occurrence (yes vs no) and group (chronic pain vs healthy control) were set as between-subjects factors. The time range between the 2 measurements was set as covariate. Moreover, two-way ANCOVAs were conducted to compare prepandemic personality factors assessed by Neuroticism, Extroversion, Openness Five-Factor Inventory\textsuperscript{22} between participants who had nonspecific COVID-19 symptoms and those without the symptoms. The perception of COVID-19 symptoms and group were treated as between-subjects factors while the time range between the 2 measurements was treated as covariate. Finally, Spearman correlations were conducted to examine the associations among prepandemic NEO personality factors, anxiety, depression, fear of COVID-19, and number of COVID-19 symptoms.

Cohen\textsuperscript{d} and 95\% confidence intervals (CIs) are reported for all the results. Outliers in the number of nonspecific COVID-19 symptoms were also considered by using the Tukey formula: Upper = Q3 + (2.2 × (Q3 – Q1)); Lower = Q1 – (2.2 × (Q3 – Q1)). Q1 and Q 3 equal 25\% and 75\% percentiles, respectively.

All analyses were conducted using SPSS version 26, and the level of significance was set at \( P < 0.05 \).

3. Results

3.1. Anxiety and depression

When comparing mood and depression between prepandemic and Stay-at-Home time points, we found that anxiety and depression worsened in both healthy participants and participants with chronic pain (anxiety: main effect of time: \( F_{1,69} = 21.88, P < 0.001 \), main effect of group: \( F_{1,69} = 1.88, P = 0.175 \); depression: main effect of time: \( F_{1,69} = 5.65, P = 0.020 \); group: \( F_{1,69} = 6.46, P = 0.013 \), Fig. 1A, B).

Prepandemic neuroticism (\( \beta = 0.57, P = 0.003 \)) and openness to experiences (\( \beta = 0.27, P = 0.013 \)) emerged as significant predictors of higher levels of anxiety during the Stay-at-Home order across participants with chronic pain and healthy participants. Baseline prepandemic anxiety was not significantly associated with anxiety during the pandemic (Table 3). For depression, neither fear of COVID-19 symptoms nor personality factors were significantly associated with depression during the Stay-at-Home order (all \( P > 0.141 \)), despite the result that greater baseline depression was a significant predictor of higher depression level during the Stay-at-Home order phase (\( \beta = 0.66, P < 0.001 \)).

3.2. Chronic pain intensity, interference, and pain coping strategies

Patients suffering from chronic pain reported a reduction of pain intensity (\( F_{1,53} = 10.52, P = 0.002 \)), with 73\% of patients reporting improved pain severity during the Stay-at-Home period (Fig. 1C). Similarly, the level of chronic pain interference during the pandemic was significantly lower (mean = 15.33, SEM = 3.66) than that before the pandemic (mean = 23.21, SEM = 3.78, \( F_{1,53} = 5.24, P = 0.026 \), Fig. 1D).

The pain coping strategies that patients used also changed significantly during the pandemic compared with the
prepandemic period. In particular, patients reported higher use of asking for assistance (eg, “asked someone to do something for me,” $F_{1,53} = 5.43, P = 0.017$), exercise or stretch (eg, “stretch the muscles in my leg,” $F_{1,51} = 5.07, P = 0.029$), and seeking social support (eg, “made arrangement to see a friend or family member,” $F_{1,51} = 8.53, P = 0.005$) during the pandemic than during the prepandemic period (Fig. 2).

Controlling for the level of somatic symptom severity assessed during the prepandemic evaluation, we found that an increase in exercise was associated with reduced chronic pain severity (Table 3). However, an increase in asking for assistance and an increase in social support were associated with a higher level of chronic pain severity (Table 3). Moreover, higher prepandemic depression was linked to greater chronic pain severity during the Stay-at-Home order (Table 3). Prepandemic depression and changes in coping strategies, when taken together, explained 31.5% of the variance of chronic pain severity during the Stay-at-Home order ($F_{11,38} = 2.58, P = 0.015, R^2$ change = 0.315).

We found that increased exercise was associated with reduced pain interference after controlling for the prepandemic level of somatic symptom severity, explaining 40.6% of variance of chronic pain interference ($F_{11,38} = 3.30, P = 0.003, R^2$ change = 0.406, Table 3).

Prepandemic NEO-related personality characteristics, baseline anxiety, and current fear of COVID-19 did not influence chronic pain severity (all $P < 0.056$) and chronic pain interference (all $P < 0.055$) during the pandemic.

### 3.3. Nonspecific coronavirus disease 2019 nocebo-like symptoms

We used the list of CDC symptoms for COVID-19 publicly available in May 2020. Current COVID-19 symptoms listed by the CDC have a few additional symptoms (eg, fatigue, nausea or vomiting, and COVID-19 tongue) that were unknown at the time the study was conducted (Fig. 3).

A total of 72 participants either tested negative or were not aware of being infected were included in the analyses. One of them was tested 4 times, and all results were negative. Three participants were tested twice, and both results were negative. Yet, when they were asked about having experienced COVID-19 symptoms, 51 of the 72 reported having experienced from
Table 3
Prepandemic predictors for anxiety, depression, and chronic pain characteristics during the Stay-at-Home order period.

Hierarchical regression model on anxiety during the pandemic assessed by STAI-II

| Blocks | Predictors | Standardized coefficient | t-value | P    |
|--------|------------|--------------------------|---------|------|
| Block 1 | Baseline anxiety | 0.205 | 1.755 | 0.084 |
| Block 2 | NEO—neuroticism | 0.566 | 3.015 | 0.003 |
|         | NEO—extraversion | 0.206 | 1.664 | 0.101 |
|         | NEO—openness to experiences | 0.274 | 2.543 | 0.013 |
|         | NEO—agreeableness | −0.172 | −1.247 | 0.217 |
|         | NEO—conscientiousness | 0.213 | 1.749 | 0.085 |
|         | Fear of COVID-19 | 0.195 | 1.813 | 0.075 |
|         | Participants with TMD vs HC | 0.020 | 0.166 | 0.869 |

Hierarchical regression model on depression during the pandemic assessed by BDI

| Blocks | Predictors | Standardized coefficient | t-value | P    |
|--------|------------|--------------------------|---------|------|
| Block 1 | Baseline depression | 0.662 | 7.393 | 0.000 |
| Block 2 | NEO—neuroticism | −0.019 | −0.151 | 0.880 |
|         | NEO—extraversion | 0.084 | 0.772 | 0.443 |
|         | NEO—openness to experiences | 0.032 | 0.335 | 0.739 |
|         | NEO—agreeableness | −0.179 | −1.495 | 0.140 |
|         | NEO—conscientiousness | 0.009 | 0.086 | 0.932 |
|         | Fear of COVID-19 | 0.112 | 1.173 | 0.245 |
|         | Participants with TMD vs HC | −0.038 | −0.338 | 0.736 |

Hierarchical regression model on chronic pain intensity during the pandemic assessed by GCPS

| Blocks | Predictors | Standardized coefficient | t-value | P    |
|--------|------------|--------------------------|---------|------|
| Block 1 | PHQ-15 baseline somatic symptom severity | 0.514 | 4.192 | 0.000 |
| Block 2 | NEO—neuroticism | 0.183 | 1.308 | 0.199 |
|         | NEO—extraversion | −0.012 | −0.069 | 0.945 |
|         | NEO—openness to experiences | 0.230 | 1.974 | 0.056 |
|         | NEO—agreeableness | −0.158 | −1.123 | 0.268 |
|         | NEO—conscientiousness | −0.044 | −0.334 | 0.740 |
|         | Fear of COVID-19 | 0.067 | 0.530 | 0.599 |
|         | Baseline anxiety | −0.099 | −0.522 | 0.605 |
|         | Baseline depression | 0.418 | 2.361 | 0.023 |
|         | Changes in asking assistance | 0.386 | 2.426 | 0.020 |
|         | Changes in exercise | −0.352 | −2.578 | 0.014 |
|         | Changes in social support | 0.277 | 2.204 | 0.035 |

Hierarchical regression model on chronic pain interference during the pandemic assessed by GCPS

| Blocks | Predictors | Standardized coefficient | t-value | P    |
|--------|------------|--------------------------|---------|------|
| Block 1 | PHQ-15 baseline somatic symptom severity | 0.412 | 3.161 | 0.003 |
| Block 2 | NEO—neuroticism | −0.193 | −1.374 | 0.178 |
|         | NEO—extraversion | −0.327 | −1.962 | 0.057 |
|         | NEO—openness to experiences | 0.200 | 1.716 | 0.094 |
|         | NEO—agreeableness | −0.168 | −1.189 | 0.242 |
|         | NEO—conscientiousness | −0.259 | −1.979 | 0.055 |
|         | Fear of COVID-19 | 0.115 | 1.327 | 0.265 |
|         | Baseline anxiety | 0.219 | 1.152 | 0.257 |
|         | Baseline depression | 0.324 | 1.821 | 0.076 |
|         | Changes in asking assistance | 0.185 | 1.160 | 0.253 |
|         | Changes in exercise | −0.283 | −2.063 | 0.046 |
|         | Changes in social support | −0.004 | −0.028 | 0.977 |

Significant results are marked as bold entries. BDI, Beck Depression Inventory; COVID-19, coronavirus disease 2019; GCPS, Graded Chronic Pain Scale; HC, healthy controls; NEO, Neuroticism, Extraversion, and Openness Five-Factor Inventory; PHQ-15, Patient Health Questionnaire—15; STAI-II, State-Trait Anxiety Inventory—Trait subscale; TMD, temporomandibular disorder.

1 (n = 28, 38%, 95% CI = 28%–51) to 10 symptoms (n = 1, 1%, 95% CI = 0%–4), refer to Figure 3. Only 2 of the 74 participants responded “yes” to the question “have you been diagnosed with COVID-19?” (1 participant with chronic pain and 1 healthy participant). Both were excluded from these analyses.

We then compared participants who reported having experienced nonspecific COVID-19 symptoms with those who did not. There was a significant group (chronic pain vs healthy participants) by perceived COVID-19 (yes vs no) by time (pre vs during the pandemic) interaction (F1,62 = 4.83, P = 0.032) on depression. In particular, we found that participants with chronic pain who reported not being diagnosed with COVID-19 but having experienced nonspecific COVID-19 nocebo-like symptoms were characterized by higher baseline depression as compared with participants with asymptomatic chronic pain (P = 0.033, Cohen d = 0.832; 95% CI = 0.176–1.489), although those 2 groups showed similar levels of depression during the pandemic (P = 0.309). For prepandemic anxiety, we found no
significant main effect of the perceived COVID-19 symptoms nor in its interaction with group or time (all $P > 0.220$).

Those who perceived symptoms had marginally lower scores for extraversion (prepandemic and during the pandemic) than those who did not experience nonspecific COVID-19 symptoms ($F_{1.67} = 3.46, P = 0.067$). Neuroticism and openness did not affect the occurrence of COVID-19 nocebo-like symptomatology (all $P > 0.252$).

For the number of COVID-19 nocebo-like symptomatology, higher baseline Depression Anxiety Stress Scale-anxiety (Spearman $r = 0.26, P = 0.027$), higher depression (Spearman $r = 0.31, P = 0.009$), and lower extraversion (Spearman $r = -0.41, P < 0.001$) were associated with a greater number of COVID-19 symptoms. Removing the outliers did not change the findings (anxiety: Spearman $r = 0.28, P = 0.018$; depression: Spearman $r = 0.29, P = 0.014$; extraversion: Spearman $r = -0.38, P = 0.001$).

In addition, the occurrence of nonspecific COVID-19 symptoms differed between healthy participants and patients with chronic pain ($X^2 = 7.30, P = 0.007$). Seventy-nine percent of those suffering from chronic pain reported having experienced at least one COVID-19 nocebo-like symptom (95% CI = 70%–88%) vs only 44% of the healthy participants (95% CI = 32%–56%). When we examined participants who showed worsening pain during the pandemic (increase pain vs decrease or sustained pain) and those who reported COVID-19 symptoms (yes vs no), we observed no overlapping between participants who showed worsening in pain and those who reported nonspecific COVID-19 symptoms ($X^2 = 0.87, P = 0.351$).

Age, sex, race, socioeconomic status (education, marital status, and annual income), and pain comorbidities (eg, irritable bowel syndrome, Table 1) did not influence the reported occurrence of the nonspecific COVID-19 symptoms (all $P > 0.175$).

4. Discussion

This study monitored pain, anxiety, and depression outcomes in a cohort of study participants who had undergone a prepandemic in-depth clinical assessment and healthy controls who were required to self-isolate during the first Stay-at-Home lockdown in the United States.

Patients suffering from chronic pain reported a reduction of pain severity and interference, with 73% of self-reported improved pain severity during the lockdown. This positive result on pain severity and interference was in contrast with the occurrence or worsening in anxiety and depression symptoms in patients with chronic pain.

Our results of pain improvements are in contrast with pain experts’ concerns positing a potential for pain worsening during the COVID-19 pandemic. A recent study reported a worsening of pain intensity and interference in 150 participants with fibromyalgia. Importantly, the study used a cross-sectional design and relied on memory of pain levels before the Stay-at-Home mandate (eg, memory biases for pain self-reports). These 2 aspects along with the different underlying pain disorders (fibromyalgia vs TMD) may explain the difference in findings with our results. Larger cohort studies are needed to draw definite answers about chronic pain–related symptoms and their fluctuations during the COVID-19 pandemic.

We observed a worsening in self-reported anxiety and depression. The combined effect of the pandemic outbreak, forced Stay-at-Home, constant mass media coverage, and high stress may have caused the occurrence of distinct symptoms (eg, abnormal illness behavior). The significant reduction of self-reported pain in patients with TMD during the forced lockdown may reflect a shift in attention from chronic pain to the time-framed situational perception of mood disorders (eg, anxiety and depression). Participants with higher baseline distressing states were more prone to experiencing higher anxiety and depression during the Stay-at-Home period. As the literature has shown in the past months, this is also true for other somatic symptoms we controlled for (eg, PHQ-15).

In addition, the current study found, as an explorative outcome, that higher prepandemic extraversion was linked to lower anxiety and lower frequency of nonspecific COVID-19 nocebo-like symptoms during the Stay-at-Home order. Extraversion, defined as a personality character that is talkative, assertive, active, sociable, and energetic, has been generally linked to positive affect and higher levels of resilience to stress. More importantly, the associations between extraversion and positive affect are independent of an individual’s social activity.

Finally, we observed that 70.8% of the surveyed participants experienced some symptoms resembling the publicly available list of symptoms for COVID-19 and that those with higher anxiety and depression and lower extraversion scores were likely to report nonspecific nocebo COVID-19 symptoms. However, our study did not include in-person severe acute respiratory syndrome coronavirus 2 tests and some symptoms (eg, headache) overlap with the TMD symptomatology. Therefore, the occurrence of nonspecific...
COVID-19 symptoms is a finding that requires caution on being interpreted as a nocebo phenomenon. Others have suggested that unspecified COVID-19 symptoms might represent nocebo responses. Nocebo effects have been linked to information disclosure about potential side effects of a treatment contributing to the occurrence of adverse effects. A treatment and an adequate control group are required to infer the nocebo effect as the cause of adverse events. Adverse events resulting from mass media and internet-based information have been reported as nocebo phenomena in the case of active drugs such as thyroxine, statins, and mass psychogenic illness after some (H1N1 influence and other) vaccinations. A recent article published during the pandemic investigated nocebo-prone behavior using the Q-No tool, a questionnaire used to predict the nocebo response, in participants with autoimmune rheumatic diseases amid the COVID-19 pandemic Stay-at-Home order period. Nocebo behaviors were detected in 51 of the 500 individuals (10.2%). Total Q-No scores were higher in the COVID-19 period compared with the pre-COVID-19 era. Among 78 patients with available Q-No questionnaires in the pre-COVID-19 era, 11 (14.1%) displayed nocebo behavior, which increased to 16 (20.5%) amid the COVID-19 pandemic. However, participants in that study were not tested for COVID-19.

This study has both limitations and strengths to acknowledge. First, the sample size is small although these results can be informative given the challenge of current pandemic. In this study, we used a sample of a small group of patients with chronic pain compared with healthy participants who agreed to participate to the study conducted within a short window (3 weeks) of the Stay-at-Home lockdown. Second, because of the paucity of testing at the time of the study (ie, limited access to testing sites and limited availability of kits at the sites), we cannot exclude the possibility that some participants were, in fact, infected with the severe acute respiratory syndrome coronavirus 2. Moreover, the patient database consists of patients with pain disorders (eg, headache or body aching) making it difficult to separate exacerbation of mood disorders from the underlying pain diseases. Third, the COVID-19 symptomology was limited at the time we conducted the study. The CDC suggested 3 classes of most common, less common, and serious symptoms; some of them (eg, in particular fatigue) were not included because they were not publicly available when we conducted this study.

In terms of strengths, it should be noted that the current study provided an important snapshot of the initial response to the COVID-19 pandemic and the first lockdown in the United States. The first lockdown extended for many months in some countries, and many countries have had repeated lockdowns and/or are currently in lockdown situations. This study was conducted when the pandemic was brand new and individual levels of uncertainty were an acute phenomenon and can inform the behavioral responses as the initial lockdowns continued while the global death toll mounted and the responses to subsequent lockdowns. Overall, our findings illuminate the possibility that the lockdown might have caused a series of symptoms. The results on coping strategies indicate a shift in attention from chronic pain to anxiety and depression. This shift suggests a need to encourage behavioral changes in lifestyle and promote a more comprehensive illness symptom management. The tendency to seek more support underlies the fact that more disabled people need and seek most support. Therefore, while promoting and encouraging a more effective access to eHealth in the United States and across countries, it is relevant to understand that psychobehavioral treatments cannot be limited to pain severity and interference. Through a broader approach, particularly pain psychology together with the multidisciplinary pain therapy, we can potentially help prevent unwanted mood disorders. The general population, patients, and healthcare providers should be aware of the disparate effects potentially caused by the worldwide distress such as the COVID-19 pandemic. Healthcare providers are in an ideal position to help educate both patients and their colleagues about the possibility of increase in anxiety and depression. People should be encouraged to practice a lifestyle that ensures regular physical activity and includes wisely selected media coverage and information sources to reduce worsening anxiety and unwanted potential nocebo-like responses while still adhering...
to the best safety practices regarding COVID-19. Patients, particularly those who tend to seek less social interactions, may benefit from social support.\textsuperscript{8,13,66} Importantly, amid the State-at-Home order of the COVID-19 pandemic, those vulnerable, especially those patients with underlying mood disorders, may require more help than they did before the pandemic.\textsuperscript{8,13}

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**References**

\[\text{1}\] Ahorsu DK, Lin CY, Imani V, Safarri M, Griffiths MD, Pakpour AH. The Fear of COVID-19 Scale: development and initial validation. Int J Ment Health Addict 2020. doi: 10.1007/s11469-020-00270-8 [Epub ahead of print].

\[\text{2}\] Amanzio M, Howick J, Bartoli M, Cipriani GE, Kong J. How do nocebo phenomena provide a theoretical framework for the COVID-19 pandemic? Front Psychol 2020;11:589884.

\[\text{3}\] Asmundson GJG, Paluszek MM, Landry CA, Rachor GS, McKay D, Taylor S. Do pre-existing anxiety-related and mood disorders differentially impact COVID-19 stress responses and coping? J Anxiety Disord 2020;74:102271.

\[\text{4}\] Bakioglu F, Korkmaz O, Ercan H. Fear of COVID-19 and positivity: a national assessment of at-risk populations. Gen Psychiatry 2020;33: e100349.

\[\text{5}\] Bani Asqar M, Jafari M, Shokri Moghadam K, Amiri M, Khosravi A, Mohseni K, Naderi M. Nocebo effects and the nocebo phenomenon. JAMA 2002;287:622–7.

\[\text{6}\] Barsky AJ, Saintfort R, Rogers MP, Borus JF. Nonspecific medication side effects and the nocebo phenomenon. JAMA 2002;287:622–7.

\[\text{7}\] Barzilai R, Moore TM, Greenberg DM, DíDomenico GE, Brown LA, White LK, Gur RC, Gur RE. Resilience, COVID-19-related stress, anxiety and depression during the pandemic in a large population enriched for healthcare providers. Transl Psychiatry 2020;10:291.

\[\text{8}\] Bavel Jv, Baicker K, Boggio PS, Capraro V, Chicocka A, Okara M, Crockett MJ, Crum AJ, Douglas KM, Druckman JN, Druy J, Dube O, Ellermans N, Finkel EJ, Fowler JH, Gelfand M, Han S, Haslam SA, Jetten J, Kitayama S, Mobbs D, Napper LE, Packer DJ, Pennycook G, Peters E, Petty RE, Rand DG, Reicher SD, Schnall S, Shariff A, Skitka LJ, Smith SS, Sunstein CR, Tabri N, Tucker JA, Linden SV, Lange PV, Weeden KA, Wohl MMA, Zaki J, Zion SP, Willer R. Using social and behavioural science to support COVID-19 pandemic response. Nat Hum Behav 2020;4:480–71.

\[\text{9}\] Beck AT, Steer RA, Carbin MG. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. Clin Psychol Rev 1996;8:77–100.

\[\text{10}\] Bloyaz G, Legros DN, Tignersrom A. COVID-19 and traumatic stress; the role of perceived vulnerability, COVID-19-related worries, and social isolation. J Anxiety Disord 2020;76:102307.

\[\text{11}\] Campbell-Sills L, Cohan SL, Stein MB. Relationship of resilience to personality, coping, and psychiatric symptoms in young adults. Behav Res Ther 2006;44:855–90.

\[\text{12}\] Chiax B, Delamont G, Guiullemassé A, Brouard B, Bibelait J-E. Psychological distress during the COVID-19 pandemic in France: a national assessment of at-risk populations. Gen Psychiatry 2020;33: e100349.

\[\text{13}\] Cheng P, Xia G, Pang P, Wu B, Jiang W, Li Y, Wang M, Ling Q, Chang X, Wang J, Dai X, Lin X, Bi X. COVID-19 epidemic peer support and crisis intervention via social media. Community Ment Health J 2020;56:796–92.

\[\text{14}\] Clauw DJ, Hauser W, Cohen SP, Fitzcharles MA. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. PAIN 2020;161:1694–7.

\[\text{15}\] Cohen SP, Baber ZB, Buvanendran A, McLean BC, Chen Y, Hooten WM, Laker PR, Wasan AD, Kennedy DJ, Sandbrink F, King SA, Fowler MW, Stojanovic MP, Hayek SM, Phillips CR. Pain management best practices from multispecialty organizations during the COVID-19 pandemic and public health crises. Pain Med 2020;21:1331–46.

\[\text{16}\] Cohen SP, Hooten WM, Phillips CR. Pain management during COVID-19 and steroids: striking a balance. Pain Med 2020;21:1731–3.

\[\text{17}\] Colloca L. Nocebo effects can make you feel pain. Science 2017;358:44.

\[\text{18}\] Colloca L, Barsky AJ. Placebo and nocebo effects. N Engl J Med 2020;382:554–61.

\[\text{19}\] Colloca L, Benedetti F. Nocebo hyperalgesia: how anxiety is turned into pain. Curr Opin Anaesthesiol 2007;20:435–9.

\[\text{20}\] Colloca L, Miller FG. The nocebo effect and its relevance for clinical practice. Psychosom Med 2011;73:598–603.

\[\text{21}\] Colloca L, Gosling J, Lowery H. Nocebo-prone behaviour in patients with autoimmune rheumatic diseases during the COVID-19 pandemic. Front Psychol 2020;11:589884.

\[\text{22}\] Costa PT Jr, McCrae RR. The revised NEO Personality Inventory (NEO-PI-R). Thousand Oaks: Sage Publications, Inc, 2008.

\[\text{23}\] Costa PT Jr, McCrae RR. Domains and facets: hierarchical personality assessment using the revised NEO personality inventory. J Pers Assess 1995;64:21–50.

\[\text{24}\] Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, Aaron JG, Claassen J, Rabbani LE, Hastie J, Hochman BR, Salazar-Schicchi J, Yip NH, Brodie D, O’Donnell MR. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet 2020;395:1763–70.

\[\text{25}\] Eccleston C, Blyth FM, Dear BF, Fisher EA, Keefe FJ, Lynch ME, Palermo TM, Reid MC, Williams ACC. Managing patients with chronic pain during the COVID-19 outbreak: considerations for the rapid introduction of remotely supported (eHealth) pain management services. PAIN 2020;161:889–93.

\[\text{26}\] Emerick T, Alter B, Jarquin S, Brancolini S, Wasan A. Telemedicine for chronic pain in the COVID-19 era and beyond. Pain Med 2020;21:1743–8.

\[\text{27}\] Escamilla EI, Ortiz LAE, Pargas JEA, Martinez AM, Botello BAL, Villa VDB, Villareal JJ. Attitudes associated with hypochondria and abnormal behavior towards illness in health science students. Psychiatr Q 2020;91:921–8.

\[\text{28}\] Faassie K, Cundy T, Petrie KJ. Medicine and the Media. Thyrroxine: an attribute of a health scare. BMJ 2009;339:b6513.

\[\text{29}\] Fragoulis GE, Evangelatos G, Arida A, Boumika V, Fragiadaki K, Karamanakos A, Kravariotis E, Laskari K, Panopoulos S, Pappa M, Mitsikostas DD, Tektonidou MG, Stikakis PP. Nocebo-prone behaviour in patients with autoimmune rheumatic diseases during the COVID-19 pandemic. Medit J Rheumatol 2020;31(suppl 2):S88–94.

\[\text{30}\] Gao Z, Lee JE, McDonough DJ, Albers C. Virtual reality exercise as a nocebo phenomenon. Front Psychol 2020;11:589884.

\[\text{31}\] Goldfarb EV. Participant stress in the COVID-19 era and beyond. Nat Rev Neurol 2020;21:683–4.

\[\text{32}\] Griswold KA, Engel-Kehl E, Ledoux A, Boivin M, Marx B. Peritraumatic experience and traumatic stress. Comprehensive guide to post-traumatic stress disorders. Cham: Springer International Publishing, 2016. p. 907–24.
