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*Brief-Report COVID-19*

# Chronic pain in the time of COVID-19: Stress aftermath and central sensitization

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**Objectives.** The COVID-19 crisis is a significant stressor worldwide. The physical and emotional condition of individuals with pain sensitization syndromes who are experiencing the pandemic may worsen. This study investigated the contribution of life changes due to the coronavirus to emotional distress in individuals with a diagnosis of chronic central sensitization pain and tested whether the associations between level of pain and sensitization were independent of or mediated by emotional distress.

**Methods.** Spanish individuals with chronic pain ($N$ = 362) completed an online survey on direct or indirect exposure to the consequences of COVID-19, pain intensity, and emotional distress. They also completed central sensitization questionnaires.

**Results.** An association was found between changes in daily routines and pain intensity, emotional distress, and sensitization scores. Correlations were found between emotional distress, sensitization, and pain intensity. Significant predictors of emotional distress were age, difficulty in receiving medical care, changes in daily routines, and diminished social support. Emotional distress did not mediate the association between sensitization and pain intensity.

**Conclusion.** Due to the COVID-19 situation, individuals with central sensitization pain syndromes may be at higher risk of developing psychological distress. Interdisciplinary interventions involving psychologists are urgently needed to provide this population with appropriate health care.

According to the European Centre for Disease Prevention and Control (2020), as of mid-July 2020, 1,592,014 cases of coronavirus infection had been reported in the European Union and the United Kingdom. The European countries with the most cases were the United Kingdom (290,133), Spain (255,953), Italy (243,230), Germany (198,963), and France (172,377). By that date, the number of deaths had risen to 179 536, of which 28 406 had occurred in Spain, which had applied one of the strictest lockdown in the world.

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**Table 1.** Descriptive statistics and Pearson correlations (N = 362)

| | *N* (%) | Mean (*SD*) | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| Changes in daily life due to COVID-19 (range: 0–5) | | | | | | | | |
| 1. Daily routines | | 3.48 (1.19) | – | .23** | .18** | .28** | .20** | .15** |
| 2. Decreased physical activity | | 3.43 (1.27) | | – | .32** | .14** | .07 | .08 |
| 3. Diminished social support | | 2.01 (1.56) | | | – | .37** | .16** | .05 |
| 4. Emotional distress (range: 2–42) | | 24.74 (8.47) | | | | – | .42** | .16** |
| 5. CS (range: 24–96) | | 63.68 (13.57) | | | | | – | .36** |
| 6. Pain intensity (range: 3–10) | | 6.41 (1.32) | | | | | | – |
| Difficulty in receiving medical care for pain | 111 (31) | | | | | | | |
| Loss of employment | 28 (8) | | | | | | | |
| Having suffered COVID-19 | 17 (5) | | | | | | | |
| Having lived with someone with COVID-19 | 19 (5) | | | | | | | |
| Death of a close person due to COVID-19 | 56 (16) | | | | | | | |

*Note*. CS = central sensitization.
**$p < .01$.

These data clearly show that COVID-19 is a global threat, unprecedented in scale, and is a significant stressor worldwide, even among individuals who are not directly affected by coronavirus.

On March 14, the Spanish government declared a state of emergency to deal with the spread of the coronavirus. Free movement was limited to essential activities between that date and May 4, when the lockdown was de-escalated to begin the return to normal life. During this period, there was breakdown in daily activity, which affected the health care of the population, including that of individuals with chronic pain (CP). This group lost access to support programs and healthcare due to the lockdown. It is estimated that one in six Spanish individuals (17%) experiences CP (Torralba, Miquel, & Darba, 2014).

It is well known that loneliness, social alienation, lack of social support, and uncertainty in health care provision are factors that can affect the prognosis and course of CP (e.g. Solé et al., 2020). Consequently, like all those experiencing the pandemic and its consequences, individuals with CP may find that their physical and emotional condition has worsened. These effects may be particularly marked in those with central sensitization (CS). The International Association of the Study of Pain has defined CS as the increased responsiveness of nociceptive neurons in the central nervous system to normal or subthreshold afferent input (Loeser & Treede, 2008). Central sensitization is characterized by generalized sensory sensitivity contributing to pain hypersensitivity, widespread pain, and polysomatization (e.g. Schrepf et al., 2018). It has been suggested that CS can modulate the development of pain in heterogeneous diseases in which the origin of nociception is difficult to ascertain, such as headache, fibromyalgia, osteoarthritis, rheumatoid arthritis, temporomandibular disorders (Woolf, 2011), low back pain, (Staud, 2011), and chronic widespread pain (Ji, Nackley, Huh, Terrando, & Maixner, 2018). All these disorders share common symptoms, of which persistent pain is the most common (Adams & Turk, 2015). Stress intolerance has also been shown to be distinctive of CS pain syndromes (Nijs et al., 2017). In fact, there is well-established empirical evidence that exposure to stressful traumatic situations increases CS (McKernan et al., 2019). Therefore, the experience of CS in individuals with CP could be affected by psychological and emotional responses to exposure to stressful events, such as COVID-19.

Thus, this study had a twofold aim: a) to investigate the contribution of life changes due to the coronavirus to emotional distress in individuals with CP; and b) to test whether the associations between level of pain and CS were independent of or mediated by emotional distress. We hypothesized that direct or indirect exposure to the consequences of COVID-19 (including the death of close ones), difficulty in receiving medical care for pain, loss of employment, changes in usual routines, decreased physical activity, and decreased social support would significantly predict the level of emotional distress. It was also predicted that emotional distress would mediate the relationship between CS and level of pain intensity.

## Method

### *Participants and procedure*

A total of 477 individuals completed an online survey. The research protocol was developed using LimeSurvey 2.0., a free software application for conducting online surveys. Participation was voluntary, and participants were not compensated for their participation. The survey that was conducted between 10 April and 30 April 2020 during the Spanish lockdown (14 March 2020 to 4 May 2020). Originally, a total of 302

associations were identified of which 52 were excluded because they did not fulfil the inclusion criteria. This information was obtained from the Spanish Pain Society and by searching for the term 'chronic pain association' on each region's website. Information on these associations is recorded on the website of the Spanish Ministry for Home Affairs. From a total of 250 Spanish chronic pain associations (i.e. not-for-profit organizations serving people affected by pain through education, information, and support advocacy), a random sample of 198 associations were invited to share the survey link between their members and via social networks during the Spanish lockdown. A letter inviting participation in the study was sent by email to the chairperson of each selected association, who was asked to forward it to all the other members. In order to reach as many participants as possible, physiotherapists from the Costa del Sol health district (Málaga, Spain) who maintained online contact with their regular patients during the lockdown were asked to collaborate in the study by sending the link to the survey to their colleagues and patients.

Participants were eligible for inclusion under the following conditions: age between 18 and 65 years, and continuous or intermittent pain of at least 3 months' duration. An exclusion criterion was a diagnosis of chronic oncological pain. The first screen of the survey site presented the consent form, and all participants were required to give informed consent to participate in the study before they continued and completed the research protocol. The study procedures complied with the Declaration of Helsinki and received institutional review board approval by the Ethics Committee of the University.

### *Materials*

Participants provided information on the following aspects: a) sociodemographic characteristics (i.e. their usual place of residence, sex, age, marital status, level of education, and employment status); b) clinical variables (i.e. primary chronic pain diagnosis, length of pain, if they were receiving medical treatment for pain, and whether the treatment had been affected by lockdown [e.g. by not being able to see a doctor or not having access to medication]); c) the consequences of COVID-19 (having contracted it, having lived with someone who had it, death of a close person due to coronavirus, difficulty in receiving medical care for pain, and loss of employment); and d) on the changes in daily life due to the pandemic lockdown (the maintenance of daily routines, decreased physical activity, and decreased social support). A 6-point Likert scale ranging from 0 (never/not at all) to 5 (always/very much) was used to ask the participants the following questions: a) whether they maintained the same daily routines as before the lockdown (i.e. *How far have you maintained your daily routines [getting up, washing up, having breakfast, lunch, and dinner at the same time?]*); b) whether their usual level of physical activity had decreased (i.e. *To what extent has your usual level of physical activity decreased by being forced to stay home?);* and c) whether they had lost social support from other people (i.e. *To what extent have you lost the social support of others [friends, family, etc] because you had to stay home due to the lockdown?*).

Pain intensity was assessed using a composite pain index of current, highest, lowest, and average perceived pain over the last 2 weeks (Jensen, Turner, Romano, & Fischer, 1999) with a rating scale from 0 ('No pain') to 10 ('Worst pain'). Cronbach's alpha coefficient was $\alpha = .83$.

Emotional distress symptoms were assessed using the 7-item stress subscale of the Spanish version of the Depression Anxiety Stress Scale (Daza, Novy, Stanley, & Averill, 2002), which comprises a 4-point Likert scale ranging from 0 ('Never') to 4 ('Usually'). The

participants had to answer according to what they had experienced over the last 2 weeks. Cronbach's alpha coefficient was $\alpha = .88$.

Severity of CS was assessed using the Spanish Central Sensitization Inventory (Cuesta-Vargas, Roldan-Jimenez, Neblett, & Gatchel, 2016). This self-report addresses 25 health-related symptoms common to CS and comprises a 4-point Likert scale ranging from 0 ('Never') to 4 ('Always'). The participants had to answer according to what they had experienced over the last 2 weeks. Cronbach's alpha coefficient was $\alpha = .88$.

### *Analysis*

All data were analysed using the SPSS software package (Windows version 22.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics and Pearson correlations coefficients were calculated. To test the first hypothesis, a multiple regression analysis was performed for the criterion variable (emotional distress). In step 1, the following variables were entered as control variables: demographic data (age, sex, marital status, level of education, and employment status) and diagnostic group (low back pain, non-specific widespread chronic pain, and fibromyalgia: these were dummy coded, with low back pain as the reference category). In step 2, variables related to COVID-19 consequences were entered. In step 3, changes in daily life due to the pandemic lockdown were entered. To test the second hypothesis, we analysed potential mediation by emotional distress in the association between CS and pain intensity (Preacher & Hayes, 2008). We also tested the indirect association between CS (predictive variable) and pain intensity (outcome variable) through emotional distress (mediator). A bootstrapping approach was used in

**Table 2.** Results of multiple regression analysis on the prediction of emotional distress

| Step and variables | Total $R^2$ | $\Delta R^2$ | $F$ for model | $\beta$ |
|---|---|---|---|---|
| Step 1 | .08 | | 4.33*** | |
| Age | | | | −.18*** |
| Sex | | | | −.01 |
| Marital status | | | | .01 |
| Educational level | | | | −.02 |
| Employment status | | | | .07 |
| WP diagnosis | | | | −.02 |
| FM diagnosis | | | | .03 |
| Step 2 | .09 | .05 | 4.47*** | |
| Difficulty in receiving medical care | | | | .19*** |
| Loss of employment | | | | .01 |
| Having experienced COVID-19 | | | | .07 |
| Having lived with someone with COVID-19 | | | | .04 |
| Death of a close person due to COVID-19 | | | | .06 |
| Step 3 | .22 | .15 | 8.29*** | |
| Changes in daily life due to COVID-19 | | | | |
| Daily routines | | | | .17** |
| Decreased physical activity | | | | −.04 |
| Diminished social support | | | | .35*** |

*Note.* WP = Non-specific widespread pain; FM = Fibromyalgia.
**$p < .01$.; ***$p < 001$.

which a point estimate of the indirect effect was derived from the mean of 5000 estimates and 95% confidence intervals were computed.

## Results

Of the initial 477 participants, only 363 had chronic primary pain related to CS: fibromyalgia (78%), chronic widespread pain (15%), and low back pain (7%). Mean pain duration was 7 years. Mean age of participants was 53.03 years ($SD$ = 8.76). In total, 92% were women, 69% were married or living as a couple, 20% were separated or divorced, 10% were single, and 1% were widowers. Regarding educational level, 43% had secondary school education, 29% had primary school education, and 27% had a university degree. Data on employment status indicated that 34% were active workers, 33% were not in employment, and 32% were retired. There were no missing data because the software survey tool used does not allow the respondent to continue when a question has been left blank. Only one multivariate outlier was identified (Mahalanobis distance $p < .001$) and removed from the final sample.

Table 1 shows the descriptive statistics and correlations between the study variables. Significant and positive correlations were found between: (a) variables considered as changes in daily life due to COVID-19 (i.e. daily routines and decreased physical activity, $r_{xy} = .23$, daily routines and decreased social support, $r_{xy} = .18$, and decreased physical activity and decreased social support, $r_{xy} = .32$); (b) changes in daily routines and decreased social support and emotional distress and CS (i.e. daily routines and emotional distress, $r_{xy} = .28$, daily routines and CS, $r_{xy} = .20$, and emotional distress and CS, $r_{xy} = .42$); (c) changes in daily routines and pain intensity ($r_{xy} = .15$); (d) decreased physical activity and emotional distress ($r_{xy} = .14$), and (e) emotional distress, CS, and pain intensity (i.e. emotional distress and CS, $r_{xy} = .042$, emotional distress and pain intensity, $r_{xy} = .16$, CS and pain intensity, $r_{xy} = .036$). Correlation values were low to moderate.

Table 2 presents the results of the multiple regression analysis on the prediction of emotional distress. The final model with all variables entered accounted for 22% of the variance in emotional distress. Significant predictors of emotional distress were age ($\beta = -.18$; $p < .001$), difficulty in receiving medical care ($\beta = .19$; $p < .01$), changes in daily routines ($\beta = .17$; $p < .01$), and decreased social support ($\beta = .35$; $p < .001$).

The results of mediational analysis showed that there was a significant direct association between CS and emotional distress (path coefficient = .26, $p < .001$) and a significant association between increased CS and higher levels of pain intensity (direct effect = .04, $p < .001$; 95% CI [.03–.05]). However, the indirect mediating association of emotional distress between CS and pain intensity did not reach statistical significance.

## Discussion

In the aftermath of crises and disasters, such as the current COVID-19 pandemic, it is well known that a negative psychological impact is a common outcome (e.g. Horesch & Brown, 2020). Such impacts could particularly affect people with CP syndromes, which are usually associated with psychological distress. Nevertheless, the results show that the predictors of emotional distress in the participants were not directly associated with the health and social consequences of the coronavirus (i.e. exposure to COVID-19, including death of close ones, and loss of employment). Instead, psychological distress among the

participants was associated with difficulties in receiving medical care, maintaining daily routines (i.e. waking up time, meal times), and loss of social support (i.e. particularly in younger participants). These difficulties are a reflection of the strict restraints imposed on the Spanish population during the coronavirus outbreak. It is also noteworthy that emotional distress scores were moderate to severe and that the mean level of pain was moderate (Krebs, Carey, & Weinberger, 2007). However, CS scores were higher than those obtained in previous research (Cuesta-Vargas et al., 2016; Mayer et al., 2012). In addition, stress was associated with CS and pain intensity, although it did not mediate the association between these variables. This is a relevant result because it shows that CS and emotional distress are independently associated with pain. Thus, both variables should be taken into account when designing interventions for these patients. It could be argued that this result may be due to the fact that the emotional distress scale used in the present study assesses tension, agitation, and negative affect rather than physiological hyperarousal. The results obtained by McKernan et al. (2019) demonstrated that the latter response, which is characteristic of post-traumatic stress, has been shown to be concurrent in individuals with a diagnosis of CS pain. Accordingly, their findings show that it is relevant to consider PTSD symptoms in the assessment, treatment, and conceptualization of CS. Unfortunately, the present study did not assess post-traumatic stress symptoms. Future studies could investigate this variable.

The interaction between biological mechanisms (i.e. allodynia, hyperalgesia, and spatial extent of pain) and psychological factors (e.g. anxiety, depression, or post-traumatic stress) is a feature of pain disorders involving CS, which is associated with worsening mental health, increased demand for health care, and poorer treatment outcomes (Mayer et al., 2012). Although COVID-19 can be highly stressful for all patients, those with CS pain syndromes may be particularly affected and at higher risk of developing psychological distress symptoms. Of note, CS pain diagnoses are strongly associated with lifetime adversity and traumatic stress (Mckernan et al., 2019). Recently, it has been pointed out that the current COVID-19 crisis should be understood as a new type of mass trauma (Horesch & Brown, 2020). Furthermore, affective and emotional factors are more relevant in CS pain diagnoses than in syndromes without CS (Schäfer et al., 2017), thus leading to poorer quality of life. Hence, some authors have emphasized the need to analyse CS pain syndromes using biopsychosocial models (Adams & Turk, 2015), which could help guide the treatment approach to be adopted with these patients. Together with biological factors, this approach should also include psychological and social variables.

A literature search found no study on all these variables in combination in patients with CS pain syndromes during the COVID-19 pandemic. Although the results of this study are limited, they may provide directions for future research. Firstly, self-report measures were used for data collection and the design was cross-sectional; thus, it was not possible to determine a cause-and-effect direction between the variables of interest. Secondly, the chronic primary pain diagnoses of the participants only included three syndromes, which limits the generalizability of these data to other CS pain syndromes. Thirdly, most of the study participants were women with fibromyalgia. Although the effect of this variable was controlled for in the analyses, future studies should be conducted with a more balanced sample of men and women and also analyse the sample by diagnosis. Fourthly, it was not possible to determine the response rate because the procedure used in the study does not allow us to establish the number of people invited versus people who chose to participate. Fifthly, the study did not assess other variables related to mental health that could also reflect the consequences of coronavirus breakdown (e.g. acute stress reaction, anxiety, and/or depression).

In conclusion, even if the health of individuals with a diagnosis of CS pain has not been directly affected by coronavirus, the pandemic outbreak and subsequent lockdown have been significant stressors. The results of the present study suggest that there is an association between negative psychological effects in patients with a CS pain diagnosis and changes in lifestyles due to the mandatory lockdown. The results also showed that CS and emotional distress are independently associated with pain. Thus, interdisciplinary interventions should be designed in which psychologists and medical care staff work together to minimize the psychological distress of patients with CS pain syndromes. These syndromes could increase the demand for health care at an extremely challenging time.

## Author contribution

Elena R. Serrano-Ibáñez (Conceptualization; Data curation; Formal analysis; Software; Writing – original draft; Writing – review & editing) Rosa Esteve (Conceptualization; Validation; Writing – review & editing) Carmen Ramírez-Maestre (Conceptualization; Validation; Writing – review & editing) Gema T. Ruiz-Párraga (Conceptualization; Validation; Writing – review & editing) Alicia E López-Martínez, Ph.D. (Conceptualization; Formal analysis; Supervision; Writing – original draft; Writing – review & editing).

## Conflicts of interest

All authors declare no conflict of interest.

## Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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