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Expert opinion in panic disorder: The impact of COVID-19-related fears, protective devices, and lockdown on panic and agoraphobia

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ABSTRACT

During the COVID-19 pandemic a perceived decline of mental well-being was reported both in people with preexisting psychiatric disorders and in people without. However, individuals with different psychiatric vulnerabilities may differ in their responses to COVID-19-related stressors. In this commentary we proposed a few considerations on possible peculiar patterns of pandemic-related behaviors or complaints in patients suffering from panic disorder (PD) with or without agoraphobia (AG). Individuals with PD may be particularly sensitive to multiple pandemic-related aspects involving respiration (e.g., wearing facial masks or COVID-19-related respiratory symptoms) that may worsen or trigger panic symptoms. In case of comorbid AG, an initial improvement of panic-phobic symptoms during the lockdown may have occurred, followed by a subsequent symptom exacerbation when the containment measures became less rigorous, possibly related to lockdown-associated negative reinforcement and impairment in consolidation of fear extinction. Personalized interventions should be offered to the patients to minimize the risk of worsening or relapse.

Commentary

Growing evidence worldwide has been pointing to the detrimental effects of the COVID-19 pandemic on mental health. Several web-based surveys in the general population documented a perceived decline of mental well-being and a significant burden of psychiatric symptoms related to the pandemic measured by different self-reported psychometric questionnaires [1, 2]. Consequently, up to approximately 63% of individuals with self-reported preexisting psychiatric disorders declared a subjective deterioration of their psychiatric condition during the pandemic in the USA, Canada, Asia, and Germany [1, 3–5]. A similar rate (i.e., 66%) emerged from a web-based survey spread by our research group in the Italian population [6]. Likewise, perceived worsening of subjective mental health or an increased burden of psychiatric symptoms were described in samples of individuals with documented psychiatric diagnoses [2, 7, 8]. Finally, we found that approximately 20% of Italians who declared to never had had clinician-diagnosed lifetime mental disorders met the cutoff scores for at least one current psychiatric diagnosis on validated self-report screening tools during the pandemic [9, 10]. Overall, this picture is consistent with the possibility that multiple pandemic-related stressors may have the potential to exacerbate existing full-blown or subthreshold psychiatric conditions, promote relapse in remitted disorders, or contribute to the emergence of new-onset psychiatric symptoms in vulnerable individuals who had never displayed clinical manifestations before. The unpredictability and contagiousness of COVID-19; its potential for life-threatening illness; concerns about one’s health and that of relatives; containment measures, such as lockdown, isolation, quarantine, and use of respiratory protective devices (RPDs); changes in lifestyle; and pandemic-related financial worries or job loss are just a few examples of such stressful events commonly shared across populations affected by the pandemic. However, it is conceivable that individuals with different psychiatric disorders or vulnerabilities differ in their specific patterns of responses to COVID-19-related stressors or display a peculiar sensitivity to some stressors rather than to others. Moreover, a portion ranging from 7% to 17% of individuals with self-reported preexisting psychiatric disorders reported a certain subjective improvement during the pandemic [6], suggesting that at least some pandemic-related conditions may have even exerted temporary favorable effects on mental health.

Thus, this commentary proposes a few considerations on possible peculiar patterns of pandemic-related behaviors or complaints in patients suffering from panic disorder (PD) with or without agoraphobia...
psychologists who are experts in anxiety disorders and work in Northern Italy, one of the areas most affected by the COVID-19 pandemic.

Patients with PD were particularly expected to complain of respiratory symptoms and somatic discomfort triggered by pandemic-related conditions due to the well-established panic–respiration connection and their peculiar sensitivity to bodily sensations. Experimental evidence has suggested the idea, unique in the field of psychiatric disorders, that subclinical alterations of basic physical functioning, mainly of the respiratory system, may play a role in the pathogenesis of panic attacks (PAs) [11]. Consequently, individuals vulnerable to PAs present a specific behavioral and respiratory hypersensitivity to hypercapnia and various other laboratory respiratory challenges (e.g., breath-holding, hyperventilation, and hypoxia). They suffer from irregular breathing patterns, impaired diaphragmatic breathing, chronic hyperventilation, and a common sensation of difficulty in breathing during daily activities [11]. Moreover, the fear of suffocation is one of their primary concerns, and they usually develop an attentional bias toward somatic sensations, proneness to catastrophic misinterpretation of normal bodily changes, and interoceptive/exteroceptive-conditioned responses. From a clinical point of view, patients with PD experience a significant burden of respiratory and physical symptoms or discomfort during PAs, as well as in several environmental situations, although the origin of these characteristics remains undefined. Moreover, they present greater physical and emotional difficulties in coping with somatic sensations and internal bodily changes compared with individuals suffering from other anxiety disorders [12,13].

As expected, we observed that patients with PD often complained about face mask-related dyspnea or sensations of smothering and asked for permission to move or remove their RPDs during psychiatric visits at our facilities, due to their peculiar sensitivity. They described similar discomfort, with urgency in moving or removing the devices, in their daily life, possibly resulting in an increased risk of contracting COVID-19. These complaints are consistent in that wearing some types of RPDs (i.e., N95 filtering facepiece respirators or full facepiece respirators) may exert, at least in experimental laboratory settings, some respiratory effects, including increased breathing resistance, carbon dioxide (CO₂) rebreathing due to CO₂ accumulation in the RPD cavity, and decreased inhaled oxygen concentration [14] to which individuals with PD are particularly vulnerable. Our preliminary data in the Italian general population during the pandemic supported this picture, showing that individuals who met the self-reported cutoff score for current PD reported significantly greater burden of physical and emotional discomfort compared with individuals with minimal or no respiratory effects or discomfort [14].

Because being compliant in RPD use is crucial to reduce risk of contracting and spreading COVID-19, strategies to decrease RPD-related discomfort of patients with PD should be identified to increase their rate of compliance, such as repeated recovery periods in safe conditions or the use of the most subjectively tolerable face masks, while remaining within safety recommendations based on the context in which the devices are used and the level of risk.

Other pandemic-related aspects may have peculiar implications for individuals with PD. In clinical experience, they complained of being particularly afraid of the occurrence of respiratory symptoms in case of COVID-19 due to their fear of suffocation and were even more frightened of being subjected to various methods of ventilation in case of severe COVID-19 for the same reason. These concerns may increase their fear of being infected or worsen their hypervigilance and attentional bias toward respiratory and somatic sensations during daily activities, which may further amplify panic symptoms. Moreover, they may perceive more intense respiratory and bodily symptoms compared with other patients in case of infection even with mild COVID-19. Considering the remarkable associations of PD with asthma or chronic obstructive pulmonary disease [16–19], it is conceivable that respiratory malfunction due to COVID-19 may have peculiar detrimental effects on panic-related respiratory pathophysiology, contributing to worsening of panic symptoms even after recovery from COVID-19. However, this idea remains speculative and needs confirmation. Finally, respiratory and somatic hypersensitivity are considered biomarkers of panic vulnerability also in people predisposed to but without clinical manifestation of panic or with subthreshold symptoms not reaching clinical significance [20–22]. Therefore, it is conceivable that wearing RPDs, hypervigilance to interoceptive somatic signals for fear of becoming infected, or respiratory and physical symptoms in case of infection with severe acute respiratory syndrome coronavirus 2 may increase the risk of new-onset clinically significant panic symptoms in vulnerable people.

In case of comorbid AG, a condition highly common in patients with PD, in our clinical activity we observed a slightly different picture with the initial improvement of panic–phobic symptoms during the lockdown or when the measures of personal movements’ restriction were very strict, followed by a subsequent symptom exacerbation when these containment measures became less rigorous. Our current clinical experience is consistent with the knowledge concerning the mechanisms of conditioning and extinction implicated in agoraphobic avoidance. It is conceivable that the aforementioned discomfort while wearing RPDs or concerns of contracting COVID-19, associated with the mandatory restrictions, resulted in a particularly pronounced decrease in daily outdoor activities in patients with PD and AG because they already employed experimental avoidance as a common strategy to escape panic-related aversive events or symptoms. In addition, as the containment measures have been applied to the entire population, avoidance behaviors have been normalized to a certain extent. Consequently, patients were less worried that others may judge them for their phobic avoidance of walking down the streets or going shopping and may have perceived avoidance as less problematic than usual and easier to be carried out. Overall, the increased avoidance behavior with prolonged periods of staying safe at home may have produced short-term subjective relief in agoraphobic patients, related to a decrease in anticipatory anxiety and situational panic–phobic symptoms. This mechanism may partly explain why the 6.2% and 21.7% of individuals with self-identified PD with AG, respectively, reported a considerable or slight perceived improvement during the first lockdown in Germany [5]. Unfortunately, the increase in experiential avoidance may act as negative reinforcement in the framework of operant conditioning, thereby hindering habituation and desensitization to the feared situations or sensations, as well as impairing consolidation of fear extinction. These processes are crucial in achieving and strengthening clinical improvement during clinician-guided exposure therapy as well as patients’ experiential activity in their daily life. Consequently, pandemic-related avoidance may result in medium- or long-term exacerbation of agoraphobic symptoms in patients with full-blown or previously partially remitted AG when freedom of movement is restored as we noticed in our patients during periods in which outdoor activities have been, at least partly, allowed again. Moreover, pandemic-related containment measures may contribute to the reacquisition of fear even in cases of previously fully remitted AG for at least two main reasons. It has been hypothesized that people vulnerable to phobic disorders may have impaired mechanisms of fear inhibition and thereby need frequent and continuous exposures to feared situations in their daily life to foster long-term extinction learning and maintain remission. Furthermore, chronic stressors are supposed to play a role in the reactivation of previously extinguished fears [23]. Consequently, both forced avoidance during the pandemic and pandemic-related prolonged distress may contribute to a possible relapse of AG in periods with less strict restriction of personal movements [11] or even after the pandemic. To decrease the risk that pandemic-related avoidance may worsen AG, clinicians should help
their patients with AG maintain adequate levels of outdoor and experiential activity even during the pandemic, by identifying and sharing feasible solutions in respect of safety rules. However, the generalizability of our current clinical experience and the plausibility of our considerations need confirmation with future follow-up clinical studies assessing AG severity in affected patients during and after the pandemic.

In conclusion, careful monitoring of patients with PD and AG during the COVID-19 pandemic is needed. Moreover, these patients may be particularly challenged by the ongoing pandemic in light of the peculiarity of panic pathophysiology and agoraphobic mechanisms. Thus, personalized strategies to decrease their discomfort should be considered and offered to the patients to minimize the risk of worsening or relapse.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclosure

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References

[1] Talevi D, Socci V, Carai M, Carnaghi G, Faleri S, Trebbi E, et al. Mental health outcomes of the covid-19 pandemic. Riv Psichiatri 2020;55:137–44. https://doi.org/10.1178/3392-3356.

[2] Hossain MM, Tasnif S, Sultana A, Faizah F, Mazumder H, Zou L, McKyer ELJ, Ahmed NU, Taamim S, Alciati A, Grassi M, Caldirola D. Mental Health, substance use, and suicidal ideation during the COVID-19 pandemic: A Canadian Multisite Study: Nouveaux deces psychiatriques pendanturant la p. Can J Psychiatry 2021;070674372098678. https://doi.org/10.1016/j.cjps.2021.06.002.

[3] Czeisler M. Emerging new psychiatric symptoms and the worsening of pre-existing mental disorders during the COVID-19 Pandemic: A Canadian Multisite Study: Nouveaux deces psychiatriques pendanturant la p. Can J Psychiatry 2021;070674372098678.

[4] Robillard R, Daros AR, Phillips JL, Porteous M, Saad M, Pennestri M-H, et al. Mental health impact of Covid-19 across different mental disorders: A study in children: ISPS. J Pediatr Psychol 2020;45:537–45. https://doi.org/10.1093/jpepsy/jsz013.

[5] Quintana JI, Dusing R, Holtmann FJ, Buhlmann U, Svadl J, Vocks S. Perceived impact of Covid-19 across different mental disorders: A study in disorder-specific symptoms, psychosocial stress and behavior. Front Psychol 2020;11. https://doi.org/10.3389/fpsyg.2020.586246.