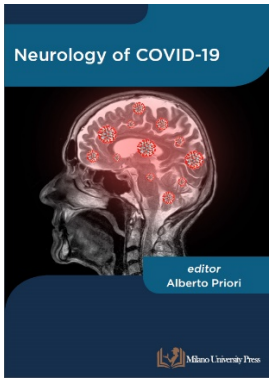

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Chapter 11. **Psychiatry and psychopathology**

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Chapter 11. Psychiatry and psychopathology

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There is a wide consensus that the current COVID-19 pandemic is affecting not only physical health, but also mental health and well-being, leading to considerable psychosocial consequences. The aim here is to give readers an update on the main research findings on the impact of COVID-19 on the principal psychiatric disorders.

Mood disorders

Mood disorders, including major depressive disorder (MDD) and bipolar disorder (BD), are common mental disorders characterized by enhanced comorbidity, mortality, and risk of suicide. Several authors suggested that people with a previous history of mood disorder are at high risk of their symptoms worsening during the COVID-19 pandemic, given their greater vulnerability to changes in daily routine due to quarantine and fear of illnesses compared to the general population[1-4]. A study by Van Rheenen and colleagues showed that depressive symptoms, anxiety, stress and general distress were heightened in patients with affective disorders compared to healthy controls, with higher rates of anxiety in patients with BD compared to those with MDD[5] (Table 11.1). Another recent study by Fiorillo and colleagues based on an online survey conducted between March and May 2020 in the Italian population highlighted that symptoms of depression, anxiety and stress significantly worsened from the week April 9–15th to the week April 30th- May 4th. Moreover, female respondents and people with pre-existing mental health problems were at higher risk of developing severe depression and anxiety symptoms[6]. In this perspective, as regards patients with pre-existing affective disorders, higher levels of depressive symptoms and general distress emerged in male patients with BD compared to females[5]. This latter finding is in contrast with several prior studies showing the opposite gender effect under non-pandemic conditions[7-9], leading to the hypothesis that male patients with BD could be presenting a worse clinical profile during the COVID-19crisis.

In addition, specific aspects of this pandemic, and of the measures necessary for its control, may be of particular concern for patients with affective

disorders, particularly regarding risk of relapse. More precisely, the course of BD is sensitive to disruption of biological and social rhythms, an effect mediated through mechanisms related to circadian rhythm regulation[10]; these alterations are a central element of BD and have been implicated in the genesis of the illness[11-13]. Some measures that have been adopted to curtail the spread of COVID-19, such as home confinement, social distancing, lockdowns and quarantine, may potentially disrupt both habitual sleep patterns and the number and quality of social contacts and activities. This could have a deleterious influence on the risk of both manic and depressive relapses[3]. In this regard, recent studies found that rigid lockdown was associated with specific sleep dysregulations in BD patients, with greater impairment in patients experiencing a depressive episode, suggesting that the social isolation, lockdown and consequent lack of emotional support might introduce biorhythm dysregulation leading to higher vulnerability to depression[14,15].

In addition, the close relationship between affective disorders and substance use, particularly alcohol use, requires consideration. During the COVID-19 pandemic, many nations have opted to continue alcohol sales for home consumption, leading to a potential increase in use in vulnerable individuals. In patients with affective disorder, this could lead to increased symptom severity, as well as adverse outcomes such as suicide[3,16]. Indeed, lifestyle behaviors are key mediators of physical and cognitive health, which is typically compromised in BD and MDD[17,18]. There is evidence that increased alcohol intake, together with sleep loss and cessation of exercise, could amplify cardiometabolic dysfunction by altering biochemical and inflammatory marker profiles[19,20]. Thus, the maladaptive lifestyle changes in response to COVID-19 might not only contribute to emotional decline and cognitive impairment, but may further compound the risk of severe SARS-CoV-2 infection and associated medical complications[21].

There is evidence of an association between positivity for coronaviruses and the risk of mood episodes. Though the significance of this association is still unclear, it may be related to the neurotrophic potential of respiratory coronaviruses or to their ability to provoke a systemic inflammatory reaction, both of which may be associated with mood dysregulations[3,22]. In particular, the presence of somatic symptoms prompt researchers to consider the psychoneuroimmunological (PNI) framework of COVID-19. COVID-19 may, indeed, cause acute respiratory syndrome with consequent release of pro- inflammatory cytokines, including interleukin (IL)-1β and IL-6 from the respiratory tract[23]; these cytokines were frequently found to be increased in MDD[23].

Finally, other issues of concern in patients with affective disorders include the general distress associated with a disease outbreak and the reduced access to treatment during an epidemic, both of which could trigger a relapse. Confinement measures considered necessary to curtail the spread of

SARS-CoV-2, may disrupt daily routines including reduced access to healthcare, therefore exacerbating affective disorders under frequent follow-up[24].

Psychotic disorders

Psychotic disorders affect 1–2% of all adults; schizophrenia[25], schizoaffective disorder[26] and acute/transient psychotic disorders[27] are the most common diagnosis. Schizophrenia involves several symptoms that differ in terms of severity of positive, negative, and cognitive impairment and the corresponding risk of the presence of depression and hostility. In addition, individuals with schizophrenia are often less educated, have lower self-control and self-care than average and inadequate understanding of their problem[28]. These elements may have influenced the greater difficulty shown by these patients in finding correct information about COVID-19 and in preventing possible contagion with appropriate behaviors[29] (Table 11.1).

In this regard, risk perception and adherence to protective measures in individuals diagnosed with schizophrenia should be of particular concern for their caregivers. A literature review by Brown and colleagues focused on the impact of successive epidemics throughout history (including SARS, MERS, Ebola, and swine flu) on psychosis. The research found that patients diagnosed with schizophrenia are less likely to be vaccinated and isolated. In addition, a positive correlation between psychotic symptoms and poor adherence with protective measures was found[30].

As regards patients presenting with a first episode of psychosis (FEP), a recent report on a 62-patient sample hospitalized between March and July 2020 compared to patients with FEP hospitalized during the same timeframe in 2019 found that the 2020 FEP patients were significantly older than patients with FEP in 2020 and presented with significantly less substance abuse. These findings suggest a major role of aging as a vulnerability factor to the stressful environment during the pandemic compared to common factors such as substance abuse[31].

From an organic perspective, people suffering from schizophrenia historically resulted more vulnerable to the adverse consequences of new infections. More than 70% of patients have experienced at least one other clinical condition, such as type-2 diabetes, chronic lung disease, or heart disease. This would increase the mortality rate caused by COVID-19 in individuals with schizophrenia[32]. Moreover, even the choice of neuroleptic therapy may expose patients to a higher risk of COVID-19 infection. For example, the use of clozapine (a second-generation antipsychotic particularly effective in the treatment of refractory schizophrenia) has been placed among the potential contraindications for schizophrenic patients due to the risk of agranulocytosis, a dangerous side effect[32].

The medium- and long-term social effects of COVID-19 may disproportionately impact people with psychosis or those at risk of psychotic disorder: social isolation, unemployment, homelessness, relationship breakdown (divorce/separation), domestic violence, and worsened physical health may all particularly affect people with psychosis, given their vulnerability to social determinants of health[33]. Moreover, the massive modifications in social networking present a surreal scenario to which it is difficult to become accustomed. For those who suffer from psychotic disorders, this new reality may exacerbate feelings of perplexity, anxiety, and paranoia. Furthermore, the current situation may be assimilated into the typical delusional contents of patients diagnosed with schizophrenia[29]. In addition, social distancing practices could have a particularly negative impact on individuals with schizophrenia. Typically, individuals with schizophrenia have on average smaller and poorer-quality social networks than the general population[34]. Thus, they may be more able to comply with, and tolerate, social distancing directives. However, social support has been associated with higher scores on recovery measures in schizophrenia and broad community support structures, including casual contacts at stores, have also been associated with improved recovery and community integration scores in schizophrenia[35]. These casual contacts have been disrupted by social distancing during the COVID-19 pandemic. In addition, social distancing may also disproportionately impact the ability of people with schizophrenia to satisfy their basic needs, given their high reliance on income support and other community services that have become more difficult to access[36].

Conversely, some recent studies have shown that COVID-19 distancing policies have not produced significant symptomatic changes for patients with schizophrenia or other serious mental illnesses[37-39], suggesting three possible hypotheses: first, an unexpected demonstration of resilience from this class of patients; second, generalized social isolation may reassure patients suffering from persecution delusions; lastly, social isolation may be absorbed within the patient's delusion[28]. Considering the above, the consequences of the pandemic in individuals diagnosed with schizophrenia are variable and subjective, and are highly dependent on each patient's symptomatology.

Table 11.1: Mood Disorders, Psychotic Disorders and COVID-19

First author, Year	Site and dates	Methods	Participants	Main findings
Fiorillo et al., 2020 [6]	Italy, March and May 2020	Online self-report questionnaire	20,720 participants, general population	12.4% of respondents reported severe/extremely severe levels of depressive symptoms and 17.6% reported anxiety symptoms. Female respondents and people with pre-existing mental health problems were at higher risk of developing severe depression and anxiety symptoms.
Ma et al., 2020 [38]	China, January-April, 2020	Online self-report questionnaires	30 patients with schizophrenia subjected to isolation; 30 patients with schizophrenia not subjected to isolation	Patients in isolation experience higher levels of stress, anxiety, and depressive symptomatology, compared to patients not in isolation. PANSS scale scores between the two groups are not significantly different, meaning that no relevant changes in schizophrenic symptomatology were detected.
Pinkham et al., 2020 [37]	USA, April-June, 2020	Online self-report survey	92 patients with schizophrenia, 56 with affective disorders	No significant changes in mood or psychotic symptoms and sleep duration emerged. A significant increase in the number of substances used emerged in patients. Patients showed a significant increase in well-being after the pandemic onset.
Van Rheenen et al., 2020 [5]	Australia, April 2020	Online self-report survey	1292 BD/ MDD, 3167 controls	Higher psychological distress in the mood disorder group vs controls. Stress and depression are further elevated in patients BD vs MDD. Higher levels of depression emerged in BD men vs BD women.
Yocum et al., 2020 [15]	USA, April 20 and May 20, 2020	Online self-report survey	413 BD patients, 147 controls	BD patients reported greater impact, with an increase in mood symptoms and a slower global improvement over time compared to healthy controls.

MDD: Major Depressive Disorder; BD: Bipolar Disorder; PANSS: Positive and Negative Symptom Scale.

Anxiety disorders

COVID-19 has been linked to increased anxiety, health anxiety, depression, stress[40-42] and suicidal ideation both in the general population[43-44] and among patients with pre-existing psychiatric disorders[45-47], particularly due to disruptions in main routines and mental health care (Table 11.2). The main consequences were represented by relapse or exacerbation of symptoms[1,4,48].

Although some studies showed that, in patients with severe/chronic mental health disorders, the COVID-19 pandemic did not exacerbate pre-existing symptoms[49-51], a study by Asmundson and colleagues focused on the impact of pandemic-related stress, scored using the COVID Stress Scales (CSS), on patients with pre-existing anxiety disorders (e.g., generalized anxiety disorder, post-traumatic stress disorder, social anxiety disorder, panic disorder)[52]. These patients exhibited higher CSS total scores and higher scores on fears about danger and contamination, socioeconomic consequences, xenophobia, and traumatic stress symptoms scales. In particular, patients with pre-existing anxiety disorders were more likely to self-isolate and to make more active efforts at coping with self-isolation distress, despite there being no evidence of any appreciable benefit for the methods they adopt to cope compared to controls.

Obsessive-compulsive disorder

Among patients with mental illness, those with Obsessive-Compulsive Disorder (OCD) showed significant clinical worsening as a result of the COVID-19 pandemic. OCD is characterized by recurrent and intrusive thoughts or images (i.e., obsessions) associated with behavioral efforts aimed at neutralizing the anxiety caused by obsessions (i.e., compulsions)[53]. Moreover, among the most common OCD symptoms is the fear of contamination leading to excessive cleaning behaviors[54,55]; indeed, frequent compensatory behaviors in OCD are compulsive hand washing, avoidance behavior with regard to touching objects considered contaminated, and cleansing rituals.

During large-scale outbreaks of infectious disease such as transnational pandemics, patients with OCD are prone to increase their dysfunctional cleaning and organizing beliefs[56,57]. The current global outbreak of COVID-19 and the consequent high fear of contamination have represented a precipitating factor for the potential increase in obsessions and compulsions, also due to the reinforced cleansing habits of patients with OCD[58] (Table 11.2). Indeed, given the high risk of contamination, better hygiene habits have been encouraged by governments and the media, generating

plausible justifications for intensifying compulsive cleaning rituals, usually considered excessive or irrational, and now legitimate and socially accepted[59]. However, this kind of information can have drastic implications for individuals with OCD, since cognitive distortions and compensatory strategies (cleansing rituals) generate plausible validation for the intensification of compulsive cleaning rituals[60], as well as excessive feelings of responsibility, and exaggerated risk assessment[61,62].

The exacerbation of OCD symptomatology has been well-documented during previous outbreaks, such as Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Influenza[63].

As expected, COVID-19-related stress has been significantly associated with OCD-like stress symptoms[41], intrusive thoughts, reassurance-seeking[64], intolerance of uncertainty, OCD symptoms, health anxiety[62], anxiety symptoms, and avoidance behaviors [65-67]. The effects of the current COVID-19 pandemic on OCD have been shown to worsen OC symptom severity, with serious clinical consequences[56,57,67-71] and changed the manifestation of OC symptoms, leading to the development of new and past obsessions and compulsions in the context of the pandemic. The onset of new and past obsessions and compulsions could be related to the need for greater control against potential contamination or the increase in spare time during the lockdown, leading to an increase in repetitive behaviors. Moreover, high rates of avoidance behaviors, mostly related to the fear of possible contamination, family accommodation, job difficulties, sleep disturbances, more psychiatric comorbidities and increased rates of suicidal ideation emerged in OCD patients during the pandemic[68].

Moreover, it is important to note that the intensification of obsessions, a sense of hopelessness, depressive symptoms and anxiety have been historically associated with high rates of suicide in individuals with OCD[72,73], and fear and stress related to COVID-19 may contribute to a rise in the risk of suicide[44,74]. Additional COVID-related factors that could potentially increase this risk include a recent increase in OCD severity, the effects of quarantine, loneliness or social isolation distress[68,75]. Furthermore, the OC dimensions of responsibility for harm and unacceptable obsessional thoughts, along with general OCD severity, have been linked to increased suicidal ideation during the pandemic[67].

Table 11.2: Anxiety Disorders, Obsessive Compulsive Disorder and COVID-19

First author, Year	Site and dates	Methods	Participants	Main findings
Asmundson et al., 2020 [52]	Canada/ USA, March-April 2020	Online self-report survey	700 patients with anxiety-related disorders, 368 mood disorders, 500 controls	Patients with anxiety-related disorders reported greater fears of danger and contamination, socioeconomic consequences, xenophobia, and traumatic stress symptoms than the other groups.
Benatti et al., 2020 [68]	Italy, March-April, 2020	Semi-structured interview conducted by telephone	123 OCD patients	Clinical worsening of OCD in more than one-third of the sample. New and past obsessions and compulsions phenotype, suicidal ideation, increased Internet checking, sleep disturbances, avoidance behaviors, work difficulties, and need of therapy adjustment emerged in OCD patients with clinical worsening.
Hao et al., 2020 [45]	China, February, 2020	Online self-report questionnaires	12 MDD patients, 19 with anxiety-related disorders, 45 with mixed anxiety and depressive disorders, 109 controls	Psychiatric patients were significantly more likely to show higher levels of PTSD, depression, anxiety, stress, and insomnia scores.
Højgaard et al., 2021 [70]	Denmark, March and April, 2020	Online self-report questionnaires	201 patients with OCD	61.2% of OCD patients reported an increase in OCD severity. Female gender, contamination symptoms, and psychiatric comorbidity were found to have a significant association with increasing OCD severity.

Khosravani et al., 2021 [67]	Iran, June 5 and October 30, 2020	Self-report question-naires	304 patients with OCD	OCD patients with OC symptom dimensions of responsibility for harm and unacceptable obsessional thoughts and severe OCD were more likely to have suicidal ideation during the pandemic.
Littman et al., 2020 [69]	Israel, March 29 and April 20, 2020	Online self-report survey	65 patients with OCD	Most OCD patients have either been unaffected by the COVID-19 crisis or have even experienced symptomatic improvement.
Matsunaga et al., 2020 [115]	Japan, April 7 and May 2, 2020	Semi-struc-tured interview	60 fully/par-tially remitted OCD patients	10% of OCD patients reported an increase in OCD severity. Patients with OCD worsening showed higher trait anxiety, depressive status, higher prevalence of generalized anxiety disorder, and contamination/washing symptoms.

MDD = Major depressive disorder; OCD = Obsessive-compulsive disorder

Eating disorders

Eating disorders (EDs) are characterized by persistent irregular eating behaviors causing a deficit in food intake or absorption, ultimately leading to a significant impairment of physical health and psychosocial functioning. anorexia nervosa, bulimia nervosa and binge-eating disorder are the most frequent EDs, and all three are characterized by irregular eating habits, along with severe distress or concern about body weight or shape[53].

In the context of the COVID-19 pandemic and the consequent lockdown measures imposed by local governments worldwide, patients both suffering and recovered from EDs have been considered by the scientific community to be at high risk of their symptoms worsening or of relapse. Scientific evidence suggested that during the first lockdown (March-May 2020) patients with EDs suffered from high levels of anxiety, along with increased dietary restriction behaviors, binge eating, purging, and exercise behaviors[76-78] (Table 11.3); a re-emergence of symptoms of Bulimia Nervosa was also reported in patients who were recovering from this condition[76]. Several factors have been suggested to play a major role in the exacerbation of ED symptoms[79]. First, food insecurity, defined by the Food and Agriculture Organization of the United Nations in 2019 as the "scarcity, reduced access to, or difficulty acquiring safe, nutritionally adequate foods"[79]; since

governments worldwide recommended limiting trips to the supermarket as much as possible, a large part of the population stormed stores to stockpile groceries, leaving shelves almost empty. Hence, even individuals from western countries, who have never experienced food insecurity before, for the first time had to face the anxiety (enhanced by media reports) of having limited access to food[80], which contributed to the so-called "feast or famine" pattern: periods of food abundance, hoarding, and overconsumption are alternated with compensatory behaviours, such as skipping meals[81]. Overall, food insecurity represents a risk factor for both the onset of an ED, and the worsening of pre-existing EDs symptoms, especially in populations from low socioeconomic backgrounds[82,83].

Second, the few opportunities for physical activity due to the closure of fitness centers and the difficulties in training outside while maintaining physical distancing. On one hand, this might lead to increased anxiety about gaining weight even in the general population; on the other hand, individuals suffering from EDs (especially Anorexia Nervosa) often use compulsive physical exercise both as a strategy to control their body shape, and as a coping method for negative emotions[84]. Therefore, when deprived of physical activity, patients with EDs often adopt other unhealthy compensatory behaviors, such as greater cutting down on calories or purging[79,85].

Third, the need to stay at home and the consequent disruption ofone's own routine, both physiological (i.e., eating and sleeping pattern) and social need to be considered[84]. Since March 2020, all non-essential workers and students have been asked to work and study from home. Family members with different time schedules were forced to reorganize spaces that they had routinely shared, which were often not adequate. On one hand, the lack of defined spaces and times to have one's own meals could negatively impact the recovery of patients with Eds. On the other hand, in order to meet the needs of the entire family, mealtimes often had to be organized several times through the day; this inevitably increased the time spent handling and speaking about food, which, in turn, may increase the risk for disordered eating behaviors[84,86]. In a psychosocial perspective, Castellini and colleagues[76] also found that the forced confinement at home often led to general domestic tensions that predicted the increase in ED symptoms in patients known for these types of disorder. In particular, patients with an insecure attachment and a history of trauma during childhood resulted more vulnerable to severe COVID-19-related post-traumatic symptomatology. Investigating the impact of social distancing on patients with EDs, it was suggested that lockdown measures might be initially thought as a potential short-term relief. In fact, having fewer social interactions also implies having fewer occasions to show in one's own body in public[79,87]. However, the authors also highlighted that, despite the short-term mitigation of interpersonal social triggers, the risk for patients with EDs to experience a worsening of their symptoms during the COVID-19 outbreak was still high, probably because social

support and adaptive coping strategies, known to be protective factors against the increase in ED symptoms, were lacking during this period[84]. Hence, it was also suggested to investigate the potential benefit of the end of the lockdown. In line with these considerations, our research group further hypothesized that the confinement at home might have represented a specific trigger for patients with EDs in terms of having more time to think about food and to compulsively gaze at one's own body in the mirror. We conducted a longitudinal study over two time points: 1) during the first lockdown in Italy - April 2020; and 2 a month after restrictions were eased - June 2020. The study aimed to assess the levels of stress, anxiety, depression, and symptoms related to post-traumatic stress disorder (PTSD) and EDs in patients with EDs. In this context, we found that patients with EDs, compared to a group of healthy controls, reported experiencing a heightened fear of losing control over eating, more discomfort at seeing their own body, and spending more time thinking about their body during the lockdown than before. We also found that, at the end of the lockdown, PTSD-related symptoms of patients with EDs significantly diminished with respect to the lockdown period, and patients reported feeling significantly better at the end of lockdown, although high levels of anxiety persisted[88].

Fourth, the restricted access to healthcare[84]. Despite the increased need for social and psychological support, healthcare services worldwide had to face the outbreak of a highly infectious disease, which led most of the hospitals to convert their departments into acute and subacute intensive care units and to block all but urgent outpatient services. In Italy, authorities were ordered to maintain full functionality of mental health and substance use services, officially recognizing inpatient and outpatient mental health services as being fundamental to the community during a global pandemic[89]. In our mental health department, second-level and third-level outpatient units, including the those dealing with EDs, were closed and switched to telemedicine programs; phone calls and video conference-based visits were organized only for emergencies or specific patient requests, and patients were encouraged to continue psychotherapy via video conference[89]. However, telehealth visits restrict the capacity to monitor weight change, vital signs, and carry out other key physiological assessments[79]. Moreover, it was reported that the discomfort of an online visit may have been a reason for avoiding mental healthcare services, especially for individuals who are at the onset of a mental health disorder[84].

In conclusion, here we have examined specific risk factors which might lead patients with EDs to experience a worsening of their symptoms during the COVID-19 pandemic. These should be taken into account when designing both therapeutic interventions tailored to the single patient, and large-scale preventive interventions.

Table 11.3: Eating Disorders and COVID-19 (experimental studies only)

First Author, year	Site and dates	Methods	Participants	Main findings
Castellini et al., 2020 [76]	Florence (Italy) T0: January – September 2019 (enrolment); T1: November 2019 – January 2020 (pre-lockdown) T2: April - May 2020 (during lockdown)	T0 and T1: self-report questionnaires, face-to face clinical interviews; T2: online questionnaires, video calls.	37 AN 37 BN 97 HC	EDs patients reported increased compensatory exercise during lockdown; household arguments and fear for the safety of loved ones predicted a higher increase in pathological physical exercise and in binge-eating episodes, respectively. In BN patients, pathways towards recovery were interrupted and previously remitted patients showed re-exacerbation of binge eating. BN patients also reported severe COVID-19-related post-traumatic symptomatology, predicted by childhood trauma and insecure attachment.
Fernandez-Aranda et al. 2020 [77]	Barcelona (Spain), first two weeks of lockdown.	Telephone survey	32 EDs patients	Most of the patients showed enhanced worries over uncertainties, for the possible negative impact of the pandemic on their work and their treatment, and fear of contagion (for themselves or their loved ones). 38% reported impairments in EDs symptoms; 52% reported additional anxiety symptoms (4 of these patients explicitly reported that stress made it difficult for them to control emotional eating).
Nisticò et al., 2020 [88]	Milan (Italy) T0: April 2020 (during lockdown) T1: June 2020 (after lockdown)	Online questionnaire	T0: 59 EDs patients and 43 HC T1: 40 EDs patients (a subset of t0)	At T0, EDs patients, compared to HC, experienced a heightened fear of losing control over eating, more discomfort at seeing their own body, and spent more time thinking about their body during the lockdown than before. At T1, in EDs patients, post-traumatic symptomatology diminished with respect to the lockdown period, and patients reported feeling significantly better, although high levels of anxiety persisted.
Phillipou et al. 2020 [78]	Australia, April 2020	Online questionnaire (national survey)	5,469 participants, 180 of whom self-reported an eating disorder history.	Since the very beginning of the COVID-19 pandemic 64.5% of the EDs patients reported more food restriction; 35.5% increased binge eating; 18.9% increased purging; 47.3% increased exercising. On the other hand, a small portion of the sample also reported decreased restricting (8%) and binge eating (8%). EDs symptoms should be strictly monitored for potential long-term consequences.

AN: Anorexia Nervosa; BN: Bulimia Nervosa; Eds: Eating Disorders; HC: Healthy Controls.

Autism spectrum disorders

The diagnostic category of autism spectrum disorders (ASDs) refers to a wide variety of conditions, affecting both children and adults, sharing the common core of "persistent deficits in social communication and social interaction across multiple contexts"[53]. These conditions can be thought of as a continuum, ranging from a severe delay in cognitive, social, and emotional development, to where individuals show selective impairment in understanding and responding to social cues, such as the tendency to avoid eye contact and a struggle in picking up cues about social context and the intentions of others, but do not present intellectual disabilities or cognitive impairment (Intelligence Quotient >70)[90]. The current literature aims at investigating how the COVID-19 pandemic and the consequent social restrictions impact on children and adults with autism, and with their caregivers.

Children with ASDs

With respect to pediatric samples, a systematic review including children with and without ASDs recently showed that, during the pandemic, children with a pre-existing diagnosis of ASDs and attention deficit hyperactivity disorder (ADHD) had a high probability of their behavioral symptoms worsening, along with presenting anxiety, depression, irritability, boredom, inattention, and fear of COVID-19[91]. It was also reported that, over the last year, children with ASDs presented symptoms resembling PTSD, in terms of increased stereotypes, aggression, hypersensitivity, and disturbance of sleep patterns and appetite[92]. However, when considering the severity of ASDs symptoms, Lugo-Marin et al.[93] also found that individuals with ASDs Level 1 (DSM-5-based) scored significantly lower in a questionnaire investigating symptoms of withdrawal and depression after the lockdown started, compared to before. Since this scale mostly investigates shyness, withdrawal, and a preference for being alone, the authors hypothesized that the drastic decrease in social demands during the lockdown had played a major role in their findings. In other words, children and adolescents with ASDs Level 1 might have partially benefited from the social distancing measures.

With respect to therapeutic interventions, although recent studies endorsed the use of video consultations for the follow-up of children with ASDs[94], White and colleagues showed that, in their sample of 3,502 children with ASDs in the United States, the majority of them experienced significant, ongoing disruptions to their therapies during the pandemic, with a consequent worsening of ASD symptoms and a heightened family distress, as reported by patients' caregivers[95]. Along the same line, Mutluer and colleagues[92] revealed that 92% of their sample, consisting of 87 individuals with ASDs in Turkey, stopped receiving special education support during this period. The authors underlined

the urgent need to develop special distance learning services also for children with special educational needs, possibly involving professionals specialized in both ASDs and trauma, in order to efficiently address the trauma-related symptomatology that emerged in their sample of children with ASDs.

Adults with ASDs

As mentioned above, moving along the autism spectrum, individuals with different degrees of symptom severity can be found. There is little literature on adult individuals with a diagnosis of severe ASDs in the context of the COVID-19 pandemic. Brondino et al. investigated the response of a sample of 18 adults with ASDs who attended a day-care center in Lombardy to new strict social routines implemented in order to keep the service running even during the lockdown. They increased the time spent performing individual physical activity, split the initial laboratory group into smaller groups, and reduced non-essential transfers to other facilities[96]. Authors assessed the patients' daily level of irritability, lethargy, social withdrawal, stereotypic behavior, hyperactivity, and inappropriate speech, and compared their findings with pre-lockdown scores. Despite the restrictions, the scores were not higher than before. These results might suggest that, when new routines are gradually and carefully introduced, people with severe ASDs might be able to adapt to them[96].

Moreover, few studies investigated the psychological impact of the pandemic on adults with high functioning ASDs. On one hand, a general increase in symptoms of anxiety and depression was reported; adults with autism showed a greater increase in worries about their work, medications and food supply, and their own safety/security, along with an increase in stress related to their loss of routine[97]. In particular, Bal et al.[98] showed that, among a sample of 396 adults with ASDs, the areas of their lives that experienced the greatest impact from the pandemic were, in order: i) employment ii) school; and iii) social life. On the other hand, a decrease in stress levels related to reduced sensory and social overload was also found[93,97]. Lugo-Marin and colleagues found a general improvement in levels of psychopathology, investigated through the Symptoms-Checklist-90-Revised (SCL-90-R), when comparing the scores of adult individuals with ASDs during the lockdown to those collected before; this was especially true in young adults (18- 30 years old). Adults aged over 30 years apparently also benefited from the social distancing measures, as demonstrated by improved scores on the SCL-90-R "Interpersonal Sensitivity", ascale that refers to feelings of inferiority and inadequacy. Only anxiety symptoms showed no significant improvement during the lockdown[93]. In fact, as reported by Oomen et al., the need to constantly adjust one's own behaviors and routines due to continuous changes in the recommendations of the authorities led several adults with ASDs to experience high levels of anxiety and distress[97].

Consistent with these findings, in our clinical practice, we observed that patients with difficulties in social interaction (e.g., patients with social phobia) often reported an improvement in their psychological well-being in relation to the imposed lockdown. This observation led our research group to hypothesize that specific groups of individuals might be able to handle social distancing better than the general population[87]. This might be the case of individuals with ASDs without intellectual disabilities. For example, previous studies showed that patients with ASDs without intellectual disabilities perform better in environments where they can work alone with a high degree of autonomy in a clearly defined and intellectually challenging job. In contrast, work settings that are highly variable from day-to-day and require teamwork and interaction with colleagues are the most challenging to secure or maintain for individuals with this ASD[99]. Preliminary results of our research, involving a sample of individuals with ASDs without intellectual disabilities and a group of neurotypical adults as control group, showed that individuals with ASDs presented significantly higher levels of stress, anxiety and depression than neurotypical adults in the first two months of the COVID-19 lockdown in Italy. However, neurotypical adults reported a higher perceived change in lifestyle during the lockdown than ASD participants. Intriguingly, with respect to the control groups, ASD individuals reported feeling more comfortable during the lockdown period in relation to the social distancing measures adopted by the Italian authorities, and said they arrived at the end of their study or working day significantly less tired during the lockdown than they had the month before (Nisticò et al., submitted paper, 2020).Trying to identify risk and protective factors for individuals with ASDs, Bal and colleagues[98] found that autistic adults who were younger, female, had a mental health diagnosis before the pandemic, and who knew someone directly infected by COVID-19, reported a greater impact of the pandemic on their life, and a corresponding greater difficulty in of coping with it. Moreover, they found that greater psychological distress was predicted by the feeling of receiving little benefit from online counselling services. In fact, as in the pediatric field and in most aspects of healthcare, services of consultation and psychological support had to rapidly reorganize and were either cancelled (as reported by the 46% of individuals interviewed by Oomen et al.[97]) or switched to remote telecommunication. Investigating the efficacy of telecommunication, Adamou and colleagues[100] reported that, in their sample of 117 adults with ASDs and ADHD in the United Kingdom, although the users subjectively found remote telecommunication to be useful, effective, reliable and satisfactory, almost half of them stated a general preference for face-to-face consultations.

Somatic symptom and related disorders

Somatic symptoms and related disorders are characterized by an intense focus on physical (somatic) symptoms that causes significant distress and/or interferes with patients' daily functioning. The DSM-5 includes in this category: i) somatic symptom disorders; ii) illness anxiety disorders; iii) conversion disorders (also called functional neurological disorders, FNDs); iv) psychological factors affecting other medical conditions; and v) factitious disorders. Recent studies have shown that the economic impact of somatic symptom and related disorders on national health systems is very high, both because of the elevated number of investigations that patients undergo (the so-called "doctor shopping" phenomenon), and because of the level of disability caused by the disorders themselves, often leading to loss of employment and need for disability benefit payments[101]. In particular, FNDs are often encountered in neurological and neuropsychiatric practice[101]. They are characterized by the presence of neurological symptoms (e.g., motor, sensory or loss of consciousness) that cannot be explained by typical neurological diseases or other medical conditions, nevertheless determining clinically significant discomfort or impairment in patients' social and/or occupational functioning[53]. FNDs encompass different phenotypes, including functional movement disorders (FMDs), in which the critical symptom relates to movement (e.g., tremor, dystonia, paralysis, gait disorders), and psychogenic non-epileptic seizures (PNES), paroxysmal events resembling epileptic attacks, although not associated with abnormal electrical activity in the brain. Several issues concerning the impact of the COVID-19 pandemic and consequent lockdown on FNDs have been raised in the literature and these will be discussed here.

The psychological impact of the pandemic on patients with pre-existing FNDs

Few studies have investigated the state of general physical and mental health in patients with pre-existing FNDs during the first lockdown (March-June 2020)[102-104] (Table 11.4). With respect to functional neurological symptoms, between 11% and 34% of patients assessed in this period reported a worsening of their symptoms; between 54% and 61% of patients reported no change in the frequency and intensity of their symptoms, and between 12% and 28% of patients felt that their symptoms had even improved during the lockdown period. Overall, an increase in stress, in poor quality of sleep, and in symptoms of anxiety was reported, which, in some cases, was associated with functional symptoms deterioration[105] but not in all[103] (Table 11.4). In an attempt to explain the stability or even the improvement of FNDs symptoms during the COVID-19 pandemic, several hypotheses were proposed. On one hand, Delgado and colleagues suggested that these findings might be caused by reduced self-monitoring, a phenomenon thought to play a significant role in the pathophysiology

of FNDs. In other words, as in everyday life, FNDs symptoms decrease when patients are distracted. During the pandemic these symptoms remained stable or even improved since patients with FNDs diverted their attention from their body to the global health crisis. On the other hand, as mentioned above, our group recently hypothesized that specific populations of patients, such as those with difficulties in social interactions, comorbid anxiety, or alexithymic personality traits, might have benefited from the lockdown, since they did not have to deal with external factors (e.g., comparison with colleagues or social relationships)[105].

Table 11.4: Pre-existing FNDs and COVID-19

First Author, year	Site and dates	Methods	Participants	Main findings
Asadi-Pooya et al., 2021 [108]	Shiraz, Iran. 2008 - 2021	Review of electronic medical records	388 PNES	94% patients were diagnosed before and 6% patients during the pandemic. PNES patients diagnosed during the COVID-19 pandemic less frequently had generalized motor seizures and had higher seizure frequencies than patients diagnosed before the pandemic.
Delgado et al., 2020 [102]	Madrid, Spain	Online survey	41 FMD	22 patients (54%) reported no change in their FMD, 5 (12%) improved and 14 (34%) worsened during lockdown. General health condition was worse or much worse in 20 patients; 15 (37%) remained stable, and 6 (15%) improved. 50% of the patients reported increased anxiety, insomnia, and lower mood, but none of these variables was associated with FMD symptoms.
Fredwall et al., 2021 [113]	Columbus, OH USA, March - June 2020	Tele-medicine program for diagnosis and support	23 PNES children and adolescents	20 patients completed their visits. At the 3-month follow up, all but 2 patients reported improvement in event frequency.
Hull et al., 2021 [106]	Houston, Texas March – October 2020	Review of electronic medical records	45 FND patients	2020: 550 new patients were evaluated; 8.2% received a diagnosis of FMD. 2019: 665 new patients were evaluated: 5.1% were diagnosed with FMD.

Mahawish et al., 2020 [107]	New Zealand January - August 2020	Review of electronic medical records	22 FND	2020: 22 patients were admitted and diagnosed with FND of whom: 9 acknowledged recent psychological stressors; a third was 70 years of age or older. 2019: 5 patients were admitted and diagnosed with FND.
Nisticò et al., 2020 [103]	Italy May 2020	Online survey	8 PNES 10 FMD 18 healthy controls	Patients with FMD showed higher levels of stress, anxiety, and symptoms related to post-traumatic stress disorder than healthy controls, but patients with PNES did not. 11.1% of patients with FND reported their functional symptoms to have worsened or to be much worsened during the previous two months, 61.1% to have remained stable, and 27.8% to have improved or to be much improved. 27.8 % of patients with FND reported their general health to have worsened or to be much worsened during the previous two months, 38.9% to have remained stable, and 33.3% to have improved or much improved.
Valente et al., 2021 [104]	Brazil, April -June 2020	Structured interviewed conducted by phone.	54 PNES	28% reported increased frequency of PNES during the pandemic; PNES aggravation was predicted by higher levels of stress, anxiety, depression, and poor sleep quality.

FND: Functional Neurological Disorders; FMS: Functional Motor Disorders; PNES: Psychogenic Non-Epileptic Seizures.

The incidence of FNDs during the COVID-19 pandemic

Retrospective review of electronic medical records of major hospitals[106,107] showed a general increase in the incidence of FNDs in 2020. In an adult and pediatric tertiary-care movement disorders clinic in Houston,Texas, USA, out of 550 new patients who were referred for evaluation between March and October 2020, 45 (8.2%) received a diagnosis of FMDs of whom 75.6% were females. This percentage is considerably higher than that of the previous years (2019), when only 5.1% of the referred patients were diagnosed with FMDs[106]. A similar increase was registered on the other side of the globe; amongst the entire population who referred to the MidCentral District Health Board in New Zealand, 22 patients received a diagnosis of FNDs between January and August 2020. These numbers are remarkable, since in the same months in 2019 only 5 patients were diagnosed with the same conditions. The authors also reported that a third of these patients were over the age of 70, leading them to hypothesize that this incidence might reflect the increasing social isolation experienced by the elderly during the lockdown. Assessing the characteristics of patients diagnosed with PNES during the COVID-19 pandemic, Asadi-Pooya and

Farazdaghi[108] from the Shiraz University of Medical Sciences,Iran, found that the patients diagnosed with PNES during the pandemic showed less frequently generalized motor seizures and had higher seizure frequency than patients diagnosed before the pandemic.

Interestingly, a case report of Piscitelli and colleagues from Italy documented the case of a 39-year-old woman who presented functional tremor in her lower limb after being diagnosed with COVID-19 and being forced into quarantine (Table 11.5)[109]. During the neuropsychiatric examination, which confirmed the diagnosis of FMD, the patient recalled that she had previously experienced a similar sudden tremor in her legs while rock climbing. This led the authors to hypothesize that her FMD might be the expression of her inability to verbally describe her feeling of anxiety which was instead expressed by a physical symptom. Similar cases of somatic symptoms and related disorders in the context of the COVID-19 pandemic have been reported from around the world[110-112] and are further detailed in Table 11.5.

The efficacy of telemedicine and online counselling services for patients with FNDs

So far, only one study conducted in a United States clinic has investigated the efficacy of telemedicine in patients with FNDs during the pandemic. Fredwall and colleagues reported that, from March to June 2020, the Psychogenic Nonepileptic Events Clinic of their hospital switched from the typical in-person visits to a telemedicine format, including a series of video-calls with neurologists and psychologists[113] (Table 11.5). Comparing data collected in this period to previously published results of in-persons visits, the authors showed that: i) there were just as many referrals to their clinic during the pandemic as before, and the rate of patients who completed the cycle of visits was also similar; ii) after 3 months, patients seen by telemedicine had similar acceptance rates, and the rate of improvement in PNES frequency even increased. However, there was a decrease in connection to psychological counselling: only 63% of the telemedicine cohort was linked with counselling in comparison to the historical control of 73%, which might be due to additional limitations in access during the pandemic. Importantly, the authors noted that visits conducted only via phone (and not video-call) were visibly less effective in both communicating the diagnosis and facilitating its acceptance among the families. Overall, telemedicine (provided with a video-call) proved to be a valid alternative to in-person visits.

Table 11.5: FNDs and SSDs emerged during the COVID-19 pandemic

First author, Year	Site and dates	Age, biological sex	Presentation	Diagnosis	Authors' comment
Buselli et al. 2020 [110]	Pisa, Italy March – May 2020	50-year-old Female	The patient (a nurse) presented with a history of fatigue and persistent dysphonia. She had previously been infected with COVID-19, which lasted about 2 months with pulmonary and extrapulmonary symptoms but, at the assessment, her test for SARS-CoV-2 was negative. No organic alterations emerged at specialist 's examination.	Given the personal vulnerability to somatization, a fact which emerged from the anamnestic interview, she was diagnosed with psychogenetic dysphonia related to COVID-19.	The authors highlight the importance of medical follow-up and psychological support for patients who tested positive for COVID-19, in particular in high-risk categories such as health care workers.
Colizzi et al. 2020 [111]	Verona, Italy, March 2020	16-year-old male	The patient, already in psychological treatment for an emerging eating disorder, presented at the Emergency Department with symptoms compatible with COVID-19. Despite testing negative for the presence of SARS-CoV-2, the patient kept presenting with psychomotor agitation and aggressivity. He responded rapidly to a low dose of antipsychotic and an antidepressant.	Based on his medical history and current presentation, he was diagnosed with SSD.	The authors highlight the importance of differentially diagnosing a possible exacerbation of a pre-existing SSD, triggered by fear of being infected, also to prevent a further burden to the healthcare system.
Jawowroski et al. 2021 [112]	Shaare Zedek Medical Centre, Jerusalem, Israel. Spring 2020	17-year-old. female	The patient, initially admitted to the ER in a rush, happily claimed to have tried to infect herself with COVID-19 by using the same thermometer as an infected patient; no evidence on the hospital security camera footage in the ER to verify her claims were founded, nor did she show any symptom compatible with COVID-19.	She was diagnosed with factitious disorder with underlying alexithymia.	The authors hypothesized that her feigning of illness might have been motivated by an unconscious need for the emotional support, she would have received as a COVID-19 patient.

Piscitelli et al. 2020 [109]	Italy, March – May 2020	39-year-old. female	The patient (a nurse), with no history of psychiatric disorder, was infected with SARS-CoV-2 and, while in quarantine, developed a lower limb tremor with variable frequency and amplitude, with abnormal movements while sitting, walking and at rest. No tremor in the upper limbs or in the cephalic district emerged; neurological and instrumental examination were normal. She showed entrainment phenomenon and effect of distractibility on the intensity of movement disorder. After testing negative for COVID-19, tremor intensity and frequency decreased.	She was diagnosed with FMD.	Since the patient recalled that she had previously experienced a similar sudden tremor in her legs while rock climbing, the authors hypothesized that her FMD might be the expression of her inability to verbally describe her feeling of anxiety which were instead expressed by a physical symptom.

FND: Functional Neurological Disorders; FMS: Functional Motor Disorders; SSD: Somatic Symptoms Disorder.

Functional neurological symptoms and COVID-19 vaccinations

Kim and colleagues[114] recently published a paper commenting on the news reported by newspapers and circulating on social media that at least one patient received the diagnosis of Conversion Disorder after experiencing continuous movement of the trunk and limbs, along with walking difficulties, after receiving the first shot of COVID-19 vaccine. The authors reminded the readers that FNDs can actually be triggered by emotional and/or physical events, including surgical procedures and vaccinations, but these cannot be considered the direct cause of FNDs. In other words, the substances contained in the vaccine cannot cause FNDs [114].

In conclusion, during the first year of the COVID-19 pandemic, the incidence of FNDs significantly increased with respect to previous years. The majority of patients with pre-existing FNDs reported no change in the frequency or intensity of their symptoms, although a global increase in stress, poor quality of sleep and symptoms of anxiety was reported. Telemedicine appears to be a promising alternative to in-person initial consultation. In the near future, the efficacy of online counselling for psychological distress should be further investigated.

Take-home message

- The current COVID-19 pandemic is having a major impact on mental health and well-being, both in the general population and in patients with pre-existing psychiatric symptomatology.
- Strict lockdown measures, leading to disruption of individual physiological and social routine (i.e., less social support, altered sleeping and eating patterns, etc.) are associated with higher risk of worsening of and relapse of mood, eating and psychotic disorders.
- The high fear of contamination and reinforced cleansing habits are severe precipitating factors for obsessions and compulsions. As in previous epidemics, individuals with obsessive-compulsive disorders showed a significant clinical worsening during the COVID-19 pandemic, and must be considered at high risk of suicide.
- Individuals with difficulties in social interaction (such as adults with high functioning autism spectrum disorders) showed, on one hand, a general increase in symptoms of anxiety and depression but, on the other hand, a decrease in stress levels related to reduced sensory and social overload.
- With respect to previous years, in 2020, the incidence of somatic symptom disorders and functional neurological disorders significantly increased; this might be due to paying greater attention towards one's own body in the context of the pandemic.

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