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It is our pleasure to present a new issue of the Mood Disorders Journal. Adding to the immense challenge implied in publishing the journal on the University of Chile's Psychiatric Clinic's website, comes our long-time aspiration of presenting our authors and readers with a bilingual edition in both English and Spanish. This is a great leap that will allow us to reach a greater number of readers and encourage academics and researchers to publish in our journal, leading to the journal being more frequently cited in the future.

The English version has been a milestone. It has been very well received by our readers and, as noted, by those who contribute with their articles.

This issue is dedicated to the most significant health challenge humanity has seen in the last 100 years: the emergence of the SARS COVID-19 virus, of which we now know not only its effects on the health of the entire human population but also its economic, social and cultural repercussions. The full consequences of its effects are not yet apparent, although they will undoubtedly impact the way of life for everyone on Earth, regardless of their ideas and beliefs (where no country has freed itself from this plague of pandemic scope.)

Due to the impact of this pandemic, most of the articles are linked to this topic. In this light, we present a study addressing which challenges and opportunities COVID-19 poses for mood disorders. Another interesting article refers to teleworking through digital means in the context of the pandemic, and a selected clinical case addresses the link between COVID-19 and mood disorders. We think that these articles will stimulate your interest concerning the enormous challenge that the pandemic currently poses for mental health in general and for mood disorders in particular.

This issue sums up by revisiting topics of interest, such as physical activity in the treatment and recovery of bipolar disorder —a very relevant indication for any patient with this clinical picture. Non-pharmacological measures like these can be of great help to the patient. A review of the mental health of university students allows us to understand the potential difficulties these students have in both acquiring knowledge and developing more comprehensively as people within the university environment.

Psychological therapies have been proven successful in synergizing bio-medical treatments. A review of this comprehensive approach is presented in order to illustrate the best evolution in patients. This approach seeks to reduce symptoms and a full reincorporation of the subject, considering aspects of their psychic and organic life, which achieve a functional remission thanks to this complete therapeutic response.

We must also share that the Bipolar Disorder Unit (BDU) at our University Psychiatric Clinic began a diploma program aimed at non-psychiatric mental health professionals, which has been very well received and has a large number of students. This diploma program responds to the concerns of psychologists and other professionals related to the treatment of mood disorders. This first version, like all the previous ones, will allow the best final works to be published in our journal.

In addition, we will soon begin the fourth version of the diploma program in mood disorders aimed at psychiatrists-- this time with an international scope, where six leading foreign specialists will be integrated

as instructors. We hope that colleagues from other Latin American countries will join us in this new initiative that crosses our borders due both to its faculty and to the ease of connectivity that psychiatrists and students from other countries will have.

We hope that this issue will be of interest to you and that our national and international diploma programs meet the expectations of academic excellence typical of our beloved University of Chile, which shelters us in its over a-century-old classrooms.

The Editors

Considerations regarding physical activity in bipolar disorder, mechanisms, recommendations, and limitations

Antonio Morales R.[1]

ABSTRACT

There is a long history of recommendation of physical activity for the maintenance of well-being and health in the history of medicine, progressively generating more and more specific recommendations for the specific management of some pathologies in accordance to new knowledge. In recent decades, a significant amount of literature addressing the impact of physical activity in Bipolar Disorder (BD) has been published, where it is proposed that some pathophysiological changes could be positively modified with physical activity--suggesting some mechanisms for this, as well as helping to manage somatic comorbidities and some psychosocial difficulties generated in this group of patients. Some aspects of the multidimensional relationship between physical activity and bipolarity, suggested change mechanisms, limitations, and suggestions for prescription in the clinical management of patients are reviewed in this work.

Keywords: *physical activity, exercise, bipolar, sport.*

INTRODUCTION

For several years now, there is knowledge that physical activity is recommended for the maintenance of health in a global way, with progressive development in increasingly precise recommendations in terms of frequency, duration, intensity, and type of exercise. There is a history that physical activity has been integrated since ancient times to the vision of health and well-being. Around 600 AD, Susruta, a renowned doctor from Benares (India), already mentioned the importance of physical activity in his university classes, in addition to recommending it to his patients at a specific intensity and time of execution, with an evaluation complete medical prescription prior to prescription, and alerting them to the risks of excessive physical activity. Since then, there are medical records in different civilizations perfecting the indication of physical activity for the maintenance of health and the treatment of diseases. Hippocrates is recognized as the first doctor on record to indicate, as a detailed written prescription, physical activity to a patient.[(1)]

Currently, the World Health Organization suggests the performance of 150 minutes of moderate aerobic activity or 75 minutes of intense aerobic activity per week for the maintenance of the health of the population at a global level[(2)]. On the other hand, the American College of Sports Medicine, in conjunction with the American Heart Association, suggests the practice of 150 minutes of moderate aerobic exercise per week, in sessions of 30 minutes for five days a week for individuals between 18 and 65 years of age[(3)]. These recommendations have been linked to a favorable and

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important impact on morbidity and mortality in the general population, mainly in metabolic, cardiovascular, mental, and oncological diseases, and general well-being, among others.[3]

When we approach the relationship between physical activity and mental health, it is possible to observe how there is a growing interest in the medical literature to know the dimension of its impact on the appearance, course, and treatment of mental illnesses, as well as the specific profile of recommended activity according to patient and pathology in terms of quality, time and intensity. Additionally, it is suggested that clinicians work in a very structured manner when prescribing physical activity to their patients. An example of this is the 5A model —Evaluate, Advise, Agree, Assist and Organize— a model developed to program physical activity in a health context.[4]

Within this growing concern for physical activity in healthcare, the interest in studying and knowing its impact in multiple dimensions in Bipolar Disorder (BD), its actual effect, its probable mechanisms, the best ways to prescribe it from a clinical practice standpoint, in addition to its problems and limitations in relation to current knowledge and other aspects associated with it, on which this text will be focused.

Exercise and bipolarity, multidimensional relationships

There has been a growing interest regarding the impact of physical activity on BD; this due, among other reasons, to the good results published concerning other mental illnesses studied, such as major depression and different anxiety disorders[5].

It is important to note the absence of multicenter and randomized clinical studies exploring the impact of physical activity on the symptomatic course of BD[6]. Despite this, some international guidelines, such as the Bipolar Disorder guide of the *National Institute for Health and Clinical Excellence*[7], already mentions physical activity as a recommendation for this group of patients. However, it appears in a general way and with little operational clarity. Instead, it focuses on lifestyle changes and the management of comorbidities, without mentioning the impact or indication of its scope in relation to the symptomatic nuclei of the disease and without references in terms of frequency, type, and intensity of exercise, thus imprecise its use in medical practice. In the previous version of this same guide, the following reference was also made: “Although exercise can be a healthy way to use excess energy in a person with mania and a helpful distraction, it could further awaken the body physiologically, increasing energy, social contact, and self-efficacy, exacerbating manic symptoms and potentially increasing cardiovascular stress “, suggesting that the practice of physical activity could even have a deleterious effect in specific phases of the disease[8].

In the context of this multidimensional relationship, a potential bidirectionality could also be deduced. An example of this is the relationship between groups of athletes who practice certain types of sports, particularly extreme or high-risk sports, with a higher prevalence of bipolarity, as suggested by a study by Dudek et al., where one-third of male and female athletes women surveyed had high scores on *the Mood Disorder Questionnaire.* The performance response in high-performance athletes, according to mood phases, has also been documented[9]. It is in this same group where it has also been pointed out that sports practice and high-demand training could hinder the correct diagnosis due to the tendency to normalize behavior and the high level of energy they display, also posing that the amount of energy could be an indicator of the course of the disorder[10].

Regarding the possible effects of exercise

on the course of BD, physical activity has been referred to as a "double-edged sword", mentioning, as previously stated, some possible harmful effects of exercise in specific cases. This is due to publications that postulate a certain relationship between increased physical activity and the facilitation of manic or hypomanic phases in some groups of patients through qualitative studies that analyze patients' individual experience around physical activity[11]. It is noteworthy to mention that, in these same qualitative analyzes, it is indicated that exercise has also produced a calming effect in the same mood phase (mania or hypomania), which has suggested that the prescription of exercise in bipolar patients should be individualized, such as in other diseases, considering the patient's previous experience with physical activity. Its follow-up and compliance could provide significant value in the evolution of BD.

In the relationship between mood phase and physical activity, the interaction between this and the trigger of depressive phases has also been studied. Interestingly, a decrease in physical activity has been reported in bipolar patients with a history of frequent physical activity: it could facilitate the appearance of depressive episodes, as published by Proudfoot et al., where, through a semi-structured interview in 209 people with a clinical diagnosis of BD between 18 and 30 years of age, different triggers were sought according to mood phase, describing among the triggers of depressive episodes, the reduction or cessation of physical activity[12].

Various scientific publications have surfaced in recent years studying another aspect that has an impact on the indication of physical activity in bipolar patients, that is, the essential somatic comorbidity associated with this group, where excess malnutrition and metabolic and cardiovascular pathologies appear in the first plane of diseases, and where, also, the practice of physical activity already has greater validity and strength of recommendation[13][14]. It is interesting to consider that some of these aspects, such as excess malnutrition, have been linked to worse treatment outcomes in patients with BD[15]. It is also known that bipolar patients have a mortality rate two to three times higher compared to the general population[16].

Additionally, there is more evidence regarding lifestyle and treatment in bipolar patients. It has been reported that bipolar patients may show higher indicators of a sedentary lifestyle than the general population, as well as other problems related to lifestyle, which are added to the side effects of various drugs widely used for the control and management of the disease, such as mood stabilizers and antipsychotics, which are associated with metabolic and cardiovascular alterations, especially if they are considered to be indicated for prolonged periods, reinforcing the indication to consider the prescription of physical activity as routine in this group of patients[17][18].

Concerning the impact of physical activity on the symptoms of BD and its phases, one of the first studies to address this issue was conducted by Ng et al. in 2007, wherein a retrospective study performed in a small sample of hospitalized patients with the diagnosis of BD who were invited to participate in a walking group during their hospital stay voluntarily. The study compared the results with the group of patients who did not participate and observed a favorable impact on those who participated in the intervention, measured through a scale that evaluated anxiety, depressive and stress-related symptoms, obtaining an improvement in all the evaluation subscales[19]. Despite the methodological limitations of the study, these results stimulated interest in knowing the scope of physical activity

in the disease beyond the indications associated with comorbidities and general recommendations for well-being in health.

The importance of individual perception regarding the benefit according to the type and scenario of physical activity chosen has also been pointed out. Suto and collaborators, in a qualitative study, evaluated different strategies used by patients with a diagnosis of BD to maintain adequate control of their disease, highlighting physical activity as a widely used strategy, where the participants also referred to how the scenario where they practiced sports (for example, outdoor sports) and the type of exercise was important to achieve that goal according to their experience[20].

Another aspect studied is the regulatory effect of physical activity on sleep, with an improvement in sleep quality[11], also establishing a two-way relationship between physical activity and sleep quality, influencing positive or negative one over the other[21]. It is also known that poor sleep quality is related to the appearance of somatic comorbidities (coronary heart disease, cerebrovascular disease, diabetes, obesity, among others[22] frequent in bipolar patients. Therefore, the intervention of physical activity could improve both aspects related to comorbidities and factors that influence or manifest changes in bipolarity itself.

In addition to the intrinsic effect proposed on mood and comorbidities, continuous physical activity can provide structure to the day and motivation, especially when finding a type of physical activity in which they feel committed, and its practice is gratifying, with the appearance in short-term exercise, pleasant sensations linked to well-being. As it has been indicated in some reports in the general population[23][24], this allows integrating it in such a way that it helps to organize the day better, optimize community networks, and maintain motivation for the future, often with a new argument to advance recovery.

Physiological and neurobiological mechanisms proposed in the interaction between physical activity and bipolarity

Multiple physiological and neurobiological mechanisms have been studied to understand the multidimensional scope that physical activity could have in bipolar patients. One of them is the serotonergic system, which is due to evidence suggesting a decrease in the central activity of this neurotransmission system in depressive phases and also in euthymia[25]. Additionally, a study conducted by Drevets et al. using Positron Emission Tomography observed a decrease in the binding potential of the 5HT1A receptor in the raphe, hippocampus, and amygdala, which was more significant in the group of bipolar patients and patients with major depressive disorder with a history of a bipolar family[26]. In addition, in relation to the same serotonergic system, it is proposed that muscle activity requires the absorption of branched-chain amino acids. They usually compete with tryptophan, the precursor to serotonin, which is transported across the blood-brain barrier. By reducing the number of competitive amino acids through muscle absorption, aerobic exercise increases the chances that tryptophan will cross the blood-brain barrier and, therefore, can increase serotonin in the brain.[27]. It has also been observed, through studies with the intracerebral dialysis technique, an increase related to the physical activity of extracellular serotonin and its acid metabolite indoleacetic 5- hydroxy in various brain areas, including the hippocampus and cerebral cortex[28].

In the dopaminergic system, a state of hyperdopaminergia has been hypothesized in manic states, specifically elevations in the availability of D2 and D3 receptors and an overactive reward processing

network. In the case of depressive states, although there is abundant literature on the importance of the dopaminergic system in Major Depression, there are no consistent findings in the depressive states of bipolar patients, as published by Ashok et al. in a systematic search of postmortem, pharmacological, and in-vivo neuroimaging studies.[29] Aerobic exercise has shown, in different animal studies, an increase in dopamine levels in the striatum, hypothalamus, midbrain, and brainstem, which reinforces the idea of the positive effect of physical activity, especially aerobic activity in mood and cognition.

The role of phenylethylamine, an endogenous neuroamine, has also been studied. It is selectively metabolized by monoamine oxidase B into phenylacetic acid, which is measurable in urine and has been associated with physical energy, mood, attention, and possesses an action in noradrenergic and dopaminergic synapses. Additionally, it has been observed that it tends to decrease its values in urine in unipolar and bipolar depressed patients. In a study conducted by Szabo and collaborators, they measured phenylacetic acid levels in men with a history of previous regular physical activity, after 30 minutes of moderate physical activity to 70% of the total cardiac capacity, observing a significant increase of this in urine in relation to the same group when they did not perform physical activity[30].

In the hypothalamic-adrenal pituitary axis, significant abnormalities are reported in bipolar patients and patients with unipolar psychotic depression. It has been determined that up to half of depressed bipolar patients fail the cortisol suppression test with dexamethasone, suggesting an altered relationship in negative axis feedback. Also, in postmortem studies, a reduction in glucocorticoid receptor messenger RNA expression has been observed in brain tissue samples from bipolar patients[31]. In addition, it has been published that regular physical activity allows the possibility of reducing the rise in cortisol in situations of high psychosocial stress[32].

A possible role for endocannabinoids has also been studied, due to their similar psychological effects, such as anxiolysis, sedation, and feelings of well-being. There is a high density of type 1 endocannabinoid receptors in the frontal cortex, amygdala, hippocampus, and hypothalamus. A single session of physical activity at 70% - 80% of maximum heart rate delivers an optimal increase in endocannabinoids. One of the most critical endocannabinoids in relation to exercise would be Anandamide. This endocannabinoid easily crosses the blood-brain barrier and is central to the benefit of aerobic activity on mood. It is produced both centrally and peripherally, tends to decrease under psychosocial stress and to increase after physical activity, and it would also have an essential role in anxiety and depression given its regulatory effect on amygdala hyperactivity[27].

Another molecule studied is the Brain-Derived Neurotrophic Factor (BDNF), which has an essential role in the neuroplasticity of patients with BD. Its tendency to decrease in the maniacal and depressive phases of the disease has been observed[33]. One of the difficulties that could occur associated with the decrease in BDNF in hippocampal cells is the reduction of the so-called “cellular resilience”, that is, a lower capacity for resistance to noxas, such as excess glucocorticoids secondary to hyperactivity of the hypothalamic-pituitary-adrenal axis and other injuries, especially in hippocampal neurons[28]. It has been reported that an isolated session of physical activity increases BDNF levels. Likewise, in the case of those who perform continuous physical activity, this effect is more significant, and also, in this group, it tends to increase BDNF values even in

repose. Preliminarily, it has been pointed out that the amount of the positive effect of aerobic physical exercise on BDNF would be smaller in women than in men and more clearly reported at moderate to high intensity of exercise[34].

The change in the inflammatory response has also been explored, this due to a pro-inflammatory profile pattern present in bipolar patients, with a predominance of pro-inflammatory cytokines such as TNF a, Interleukin 6 and 8, in addition to a reduction of Interleukin 4, which has anti-inflammatory activity in both in manic and depressive phases. However, the role of terlequine 6 is more complex since its action could be pro or anti-inflammatory depending on the receptor to which it binds. Physical activity could cause an activation of the binding of Interleukin 6 to mainly anti-inflammatory receptors, which would have a secondary, favorable impact on the levels of BDNF and somatomedin. This is associated with the possible mechanism of reduction of cognitive damage through the reduction of hippocampal inflammation[28]. In addition, it is proposed that there could be a close relationship between physical exercise, an increase in the endocannabinoid Anandamide, and an increase in BDNF; there has been an attempt to show this by blocking cannabinoid type 1 receptor in rats, generating, as a result, a lower response to increase BDNF in them post-exercise[35].

Among the mechanisms, the positive impact of physical activity on the probable mitochondrial dysfunction present in BD is suggested, as it occurs in other diseases with mitochondrial involvement, where physical activity has shown benefit through this mechanism[36]. This mitochondrial dysfunction is proposed due to the observed alterations in brain energy metabolism, the impact of mood stabilizers on the mitochondria, the increase in deletions of mitochondrial DNA in neural tissue of bipolar patients, and the association of mutations and polymorphisms of mitochondrial DNA with bipolarity[37]. It has also been suggested that exercise could be related to the activation of a protein kinase activated by AMP, which would cause positive effects on learning, memory, neurogenesis, and gene expression associated with mitochondrial function in the hippocampus[38].

CONCLUSIONS

There is a long medical tradition that integrates the indication of physical activity as a treatment for diseases, and the case of BP should not be the exception. Although conclusive studies have not been published in this regard, there is a significant amount of literature that recommends the practice of continuous or frequent physical activity, mainly moderate or high-intensity aerobic activity, which is possible to make operative in adult patients without somatic impairment that contraindicates it, and, with the knowledge of its limitations, through the training of the patient in the measurement of their heart rate during exercise and estimating, using some highly diffused formulas in sports, such as those of Fox[39] or Tanaka[40], suggested heart rate parameters for the patient's training session, always considering a previous general medical evaluation, and investigating the absence of contraindications to performing physical exercise.

According to the information currently available, it is possible to say that it is highly suggestive that regular physical activity has a favorable impact on the control of different aspects of BD, such as the attenuation of mood and cognitive symptoms, a decrease in risk or of the impact of somatic comorbidities, as well as favoring community contact, sense of agency, and motivation regarding personal development.

The clinician must make an effort, in light of the patient's mental history, to perform a general medical evaluation of possible comorbidities and specific medical conditions of the patient, as well as the patient's previous experience with physical activity, to recommend it in a structured way, considering that frequency, intensity, time of day, relationship with food, duration and type of exercise, among other aspects, must be carried out in a personalized way, and subsequently collecting the experience, tolerance, and adherence to what is prescribed, as well as the patient's relationship with physical activity as a possible influence to mood swings. Despite the existence of certain recommendations where the appearance of favorable mechanisms for both the disease and comorbidities is explained through neurobiological and physiological theories, the prescription must be conducted in such a way as to not hinder the patient's access to it, knowing that the greatest benefits in general morbidity and mortality, they appear when passing from a completely sedentary life to initiating small changes in the sense of improving physical activity[41].

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Mood Disorders in Times of COVID-19: Challenges and Opportunities

Daniela Waissbluth P.[1]

ABSTRACT

Introduction: Less than a year after it began in Wuhan, the SARS-CoV-2 coronavirus infection has had profound repercussions worldwide. The health manifestations are varied, as are the psychological aspects involved.
Method: A bibliographic search was conducted through PubMed; articles related to mental health topics, neuropsychiatry, mood disorders, and COVID-19 were included.
Results: COVID-19 has generated mental health manifestations that are believed could persist over time, with anxiety and depression being the most significant ones reported. The virus has the ability to enter the central nervous system, causing neuropsychiatric manifestations. Patients with mood disorders, as well as health professionals and survivors of COVID-19, are presented as a risk group. Regarding treatment, special care must be taken in terms of drug interactions and possible severe adverse reactions. Lithium carbonate has properties that could be of interest as a potential coronavirus treatment.
Conclusions: The traditional working modalities of mental health teams should be changed. In mood disorders, consider aspects proper to the viral infection, as well as the psychosocial determinants. Propose suicide prevention strategies, where remote interventions become critical. In addition to the challenges, this period can be considered an opportunity to modify care paradigms and generate new research lines.

Keywords: *"COVID-19", "coronavirus", "psychiatry", "mental health", "mood disorder", "depression", "bipolar disorder", "psychopharmacology".*

INTRODUCTION

Only seven months have passed since the first cases of infection by the then called "new coronavirus of 2019", detected in the city of Wuhan, China. In February 2020, the WHO named the illness "coronavirus disease" (COVID-19) and the causative pathogen, "type 2 coronavirus causing severe acute respiratory syndrome "(SARS-CoV-2).

When we talk about dates, considering the global impact that this pandemic has had, it seems like a recent event. From this side of the world, society watched what was happening with the distance of a spectator. While thousands died in Asia and Europe, Chile, still in summer, was shocked by the repercussions of the social outbreak. However, the potential impact of the pandemic did not appear to be felt until the first weeks of March.

However, not only local challenges and

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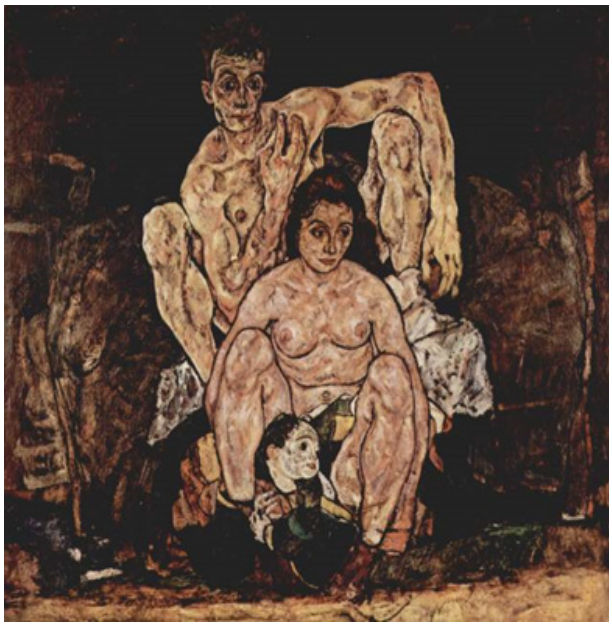
processes favored the feeling of distance from risk. Throughout history, humanity, plagued by various pandemics, seems to need historical texts to recall the notion of "biological vulnerability." The Spanish Flu—a relatively recent historical event as only one hundred years have passed since it began—was a disease that was responsible for the loss of 50 million people worldwide in less than a year and whose multiple health, economic, and historical consequences may have been overshadowed by the aftermath of humanity already struck by the ravages of war[1]. Nevertheless, there are records of survivors which account for the harsh reality of the pandemic—in a period where the immediate capacity for recording and broadcasting that we have today was not possible, with the benefits and harms that this implies. Among the tragic outcomes of the pandemic is the story of the painter Egon Schiele, known for his position as an intellectual and cultural elite, who lost his wife and unborn child to the virus, and died a few days later from the same illness. His mentor, the famous Gustav Klimt, also succumbed to the illness eight months before Schiele himself. One of the young painter's most famous works was developed the same year of his death, remaining unfinished *(Figure 1)*.

Figure 1. Egon Schiele, The Family, 1918.



Mental Health and COVID-19

The scope of the pandemic involves diverse global aspects; thus, the entire population is affected directly or indirectly. However, there are groups that evidently present a higher degree of vulnerability, whether due to biological, economic, social, professional determinants or a combination of all of the above.

The Severe Acute Respiratory Syndrome (SARS) disease caused by SARS-associated coronavirus (SARS-CoV) in 2003 generated mental health consequences in patients and families that lingered after recovery; the biological aspects (of the virus, hospitalization, medication) and psychosocial[2] were considered relevant. Psychological distress remained high for one year after infection in that SARS epidemic, while healthcare personnel had higher rates of depression, anxiety, and post-traumatic stress disorder each year[3]. Completed suicide rose, specifically in the geriatric female population, the year of the Hong Kong pandemic[4].

Experts propose four groups of particular interest due to their higher-risk potential: (I) people who have been in direct contact with the virus and the disease, (II) people with previous psychosocial and biological vulnerability (including those patients with already diagnosed psychiatric illnesses), (III) healthcare professionals, and (IV) people who follow multiple channels of information regarding the pandemic[5]. This last point opens an interesting discussion regarding the role of the media and how the globalized immediacy of information can influence health outcomes, differing in

certain areas from the course of previous global pandemics, such as the Spanish Flu.

Research in relation to the impact on mental health during the COVID-19 pandemic is still a subject in full development. The most substantive data comes from the Chinese population, with some longitudinal and case-control studies. In the general population, the levels of anxiety, depression, and stress lingered one month after the peak of new cases, and the group of adolescents and young students is proposed as the most vulnerable group[6] which is not replicated in other studies. It is suggested that the population with psychiatric pathology would suffer a greater impact than that of the general population during the COVID-19 pandemic, quantified through anxiety and depression scales[7]. Although studies are still scarce, the multiplicity of adverse factors at play make this a theoretical population at risk due to inadequate coping strategies in the face of stress, previous psychosocial problems, lack of access to timely controls during the pandemic, and difficulties in the access to regular medication, among others. The increase in depression figures could be associated with lower income, interpersonal conflicts, frequent use of the media, and less social support, and it is higher in females[8].

The call to social isolation as a measure of physical protection can be detrimental to mental health, which is why the term “physical distancing” has been preferred to “social distancing”[9]. Although they may seem like subtleties of language, it becomes relevant when considering other effective communication channels to sustain the experience of emotional containment in times of crisis, making a virtuous use of technology to maintain contact with meaningful relationships, and access to healthcare in a timely manner. In China, it has been observed that the quarantined population presents significantly higher levels of anxiety and depression than the population without mobility restriction[10]. In the particular case of Chile, a country where the issue of inequality has been at the fore in the past year, and with a large vulnerable and marginalized population, isolation also carries the stressor of a scarcity of basic goods[11].

A group of particular interest corresponds to that of healthcare professionals. The degree of exposure and risk, the experience of work overload and sleep deprivation, the making of ethically complex decisions on a daily basis, and distancing oneself from the primary support group to avoid contagion are some of the influencing factors. The prevalence of anxiety, depression, and insomnia as isolated symptoms in healthcare professionals during the COVID-19 pandemic reaches 23.2%, 22.8% and 38.9%, respectively; the figures being higher specifically in the female population and the nursing profession[12].

Considering the various mental health issues faced due to the pandemic and defining the main research priorities, The Lancet published a position paper in April with a complete bio-psychosocial approach, understanding the scopes of multiple determinants[13]. In it, they establish as immediate research priorities: (I) obtaining data on rates of anxiety, depression, and suicidality; (II) investigating support strategies for particular risk groups (pre-existing severe mental or physical illness, individuals recovered from COVID-19 infection, and people who report new psychiatric/psychological symptoms during the pandemic); and (III) develop a neuropsychological database of COVID-19 patients that allows generating standardized studies to understand the neuropsychiatric effects of the virus better.

Neurobiological Aspects: SARS-CoV-2 and the Nervous System

SARS-CoV-2 is an RNA virus, which in addition to respiratory manifestations, presents extrapulmonary manifestations, including those in the nervous system, generating neuropsychiatric conditions already documented[14], such as encephalitis, meningitis, vascular events, cognitive alterations (specifically a dysexecutive syndrome), neuro-ophthalmological alterations, and Guillain-Barré syndrome, among others. It is even suspected that a neuroinvasion at the brainstem level could be partly responsible for the great respiratory failure in these patients[15]. Regarding delirium in critical patients due to COVID-19, some authors propose underdiagnosis as a potential problem, but it is posed as a daily clinical reality[16]. Among the factors inducing delirium, the direct effect of the virus on the central nervous system and the inflammatory cascade is considered as two influential components, in addition to those inherent to any critical patient[17], which forces us to ask questions about the neurotropic mechanisms of this virus.

Past epidemics such as SARS and the Middle East Respiratory Syndrome (MERS) generated studies on coronavirus neurotropism (CoVs) in animal models; one of the consistent findings was that they all require angiotensin-converting enzyme 2 (ACE-2) as a neuronal gateway[18]. ACE-2 is expressed in multiple organs, including the brain, specifically in neurons and glia. SARS-CoV-2 uses the S1 “spike” glycoprotein that binds to ACE-2, entering the cell, and it has been seen that the affinity of SARS-CoV-2 for this receptor is greater than for other coronaviruses[19]. One line of research regarding neuroinvasion is entry through the olfactory nerve, with ECA-2 being widely distributed at the level of this sensitive epithelium, and it is known that SARS-CoV-2 generates anosmia and ageusia as a frequent symptom[20].

In sum, the mechanisms of SARS-CoV-2 in injuring the nervous system may include entry through systemic circulation, direct neuronal pathway, damage from neuroinflammation, and damage from hypoxia and vascular events, among others, having at least been clarified up to the important role of ACE-2 in cell admission[21].

Mood Disorders and COVID-19

Data on depression, bipolar disorder, and COVID-19 are still scarce, but it is suspected that there is likely to be an increase in the figures considering what happened with the SARS pandemic. Up to 36% of the patients had a low mood during the acute recovery phase, with the severity of SARS and the use of corticosteroids being associated with higher levels of anxiety and depression[22]. Long-term follow-up of survivors, even over three years, showed that 39% met the criteria for depression[23]. In the past, interest has been generated in the possible relationship between respiratory virus infections and the triggering of mood disorders, finding that seropositivity for influenza A, influenza B, and coronavirus is associated with mood disorders, without demonstrating specificity for unipolar depression or bipolar disorder[24]. It is believed that carriers of a mood disorder could eventually have a more lasting inflammatory response in viral infections due to the increase in pro-inflammatory cytokines, which is characteristic of the pathophysiology of the mood[25].

In a prospective study on COVID-19, it was seen that the severity of anosmia and ageusia was associated with higher levels of anxiety and depression[26], which again suggests the potential compromise of the central nervous system by the coronavirus.

In a study comparing current mental health repercussions in patients with previous mood disorders (either depression

or bipolar disorder) versus the general population, indicators of depression and anxiety were higher in the former group and even more so in bipolar disorder compared to unipolar depression, with bipolar men being the most affected[27].

Regarding the risk of suicide, it is presumed that the rates could increase if we consider the precedent of an increase in suicide deaths in the United States during the Spanish Flu and among older adults during the SARS epidemic[28]. So far, several cases of suicides related to COVID-19 have been reported both in the press and in scientific publications in the United States, Italy, Great Britain, India, among other countries; therefore, it is proposed that the role of the psychiatrist and mental health teams should be more active than usual in patients who are deemed to be at higher risk, such as those with a history of previous attempts, patients with active psychiatric conditions, especially if they are older adults, and health professionals[29]. In anticipation of the potential increase in suicidal phenomena, and in addition to quarantine prolongations and the psychosocial consequences that this implies, some efforts have already been proposed to conduct brief and structured interventions that specifically aim at reducing suicide risk, such as the Collaborative Assessment and Management of Suicidality (the acronym CAMS is frequently used in English) through a telepsychology protocol[30]. Psychiatry and psychology experts, therefore, support the idea of having an active approach to suicide prevention in risk populations, and, in this sense, remote interventions should have a preponderant place.

Regarding psychopharmacological aspects, greater rigor is required when prescribing and monitoring patients with mood disorders during the course of SARS-CoV-2 infection, especially considering three aspects: (I) the risks of the use of drugs common in psychiatry in critical patients, with complications in various systems; (II) the multiple pharmacological interactions existing between experimental treatment protocols and the use of certain psychoactive drugs; and (III) the potentially adverse neuropsychiatric reactions to drugs used to combat SARS-CoV-2 infection.

Given the multisystemic alterations in severe patients due to COVID-19, it is relevant to consider pharmacokinetic and pharmacodynamic aspects when prescribing and dosing. In the case of antipsychotics, special caution should be exercised in patients with cardiological alterations in the critical patient context due to the risk of QTc prolongation, and in patients with transaminase alterations due to systemic inflammation; antipsychotics with risk of hepatotoxicity should be avoided[31]. Furthermore, COVID-19 has been associated with leukopenia and lymphopenia, so starting a prescription of drugs such as clozapine or carbamazepine should be carefully considered, balancing risks and benefits[31]. Concomitantly, the use of clozapine has been associated with an increased risk of systemic inflammation and pneumonia[32].

Regarding the follow-up protocols in patients with pharmacotherapy already installed, due to the problems of access to the laboratory and the risks of contagion, it has been proposed for some drugs to postpone laboratory controls. Experts have recommended reducing the frequency of hematological monitoring with the use of clozapine every three months in patients who have been using it for more than a year and have stable white blood cell and neutrophil counts in that period[33].

Among the “off-label” uses of therapies for COVID-19, various drugs can be found, including chloroquine, hydroxychloroquine, azithromycin, lopinavir-ritonavir, favipiravir, remdesivir, ribavirin, and interferon, among others. Some of them present potentially

serious adverse reactions such as QTc prolongation, hepatitis, pancreatitis, neutropenia, and anaphylaxis[34]. In this scenario, the psychiatrist liaison must take special care to review possible drug interactions and choose a safe scheme within the possibilities.

In the subgroup of patients with a greater systemic inflammatory component, such as cytokine storm, the use of immunomodulatory drugs such as corticosteroids, immunoglobulin, and selective cytokine blocking such as tocilizumab[35] has been proposed, with known psychiatric adverse reactions, especially from corticosteroids and interferon, such as depression, mania, agitation, and suicidal reactions, among others[31].

Regarding lithium carbonate, which continues to be one of the cornerstones of treatment in mood disorders, there are specific concerns but also promising aspects regarding its use during the pandemic. There are already documented cases of patients with lithium intoxication and hospitalizations for SARS-CoV-2[36], which warns about the complications that may occur due to low fluid intake or kidney failure as part of the severity of their evolution; thus, timely control of lymphoma in patients who acquire the infection is highly relevant, adjusting doses as needed. Nevertheless, lithium has certain potential benefits worthy of consideration; it is a drug that has been shown to slow down the replication of coronavirus in animals in vitro through the inhibition of an enzyme called glycogen-synthetase kinase 3, involved in the phosphorylation of cofactors necessary for RNA polymerase[37]. Some have proposed studying lithium in microdoses for its protective effects, preventing inflammation associated with a senescent phenotype[38]. In this way, new fields of research are opened regarding the use of lithium and viral infections.

Challenges

The challenges for psychiatry during this pandemic are several. On the one hand, the need to anticipate and prepare for the increased demand for care due to the immediate and long-term mental health repercussions. In this sense, implementing an effective and efficient telepsychiatry system is presented as a highly relevant challenge[39]. Perhaps in more global terms, the challenge has to do with modifying the clinical and research work modality of mental health teams[40] from all their intervention spaces. The need to implement telepsychiatry and telepsychology platforms early and effectively, create an efficient process of dispensing and withdrawing medication to ensure continuity of treatment, intensify isolation measures in psychiatric hospitalization units, and conduct virtual psychiatric interventions[41, 42].

Another challenge is implementing multidisciplinary mental health interventions in two specific groups: healthcare personnel and patients and relatives affected by COVID-19[43]. Therefore, needs arise beyond the usual task, which will be particularly complex for psychiatry teams.

Leaving the clinical field, a pending challenge for psychiatry and scientific societies is that of broadcasting and education of the media, so that the type of information and its modes of transmission do not detract from the mental health of the population. This is a preventive strategy[44].

CONCLUSIONS

COVID-19 has come to revolutionize various aspects of daily life. For mental health teams, this implies a need to adapt at a rate seldom seen before, in order to meet the new requirements for the population and especially for groups at risk of presenting psychopathology.

Current information indicates that SARS-CoV-2 is a virus that has the ability to enter

the central nervous system and present numerous neuropsychiatric manifestations, this being a field in full development. In mood disorders, aspects of the viral infection must be taken into consideration and the psychosocial determinants involved. In psychopharmacology, special care must be taken when evaluating drug interactions and possible neuropsychiatric repercussions of new treatments for COVID-19. On the other hand, lithium carbonate has properties that could be of interest as a potential treatment for coronaviruses.

Considering this a period of crisis from multiple angles, it is also an opportunity for growth and to modify our usual paradigms of functioning, both in psychiatry and in other areas. As an example, the creation of a virtual art gallery, The Covid Art Museum, specifically dedicated to publishing works related to the pandemic. This is how creative spaces arise, which also, in part, can be considered a strategy of expression and coping during such complex times *(Figure 2)*.

Figure 2. Virtual work published in the Covid Art Museum, artist @anindianminiaturist

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Depression and psychological well-being in university students: A Theoretical Review

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ABSTRACT

The present research, of a theoretical nature, reviews studies focused on identifying the presence of depressive symptoms and their relationship with socio-demographic background in university students from national and foreign universities. At the same time, it makes a review around the concept of psychological well-being and its general characteristics in the population. The results indicate a high prevalence of depressive symptomsin university students compared to the general population and similar values among foreign and national university populations. Studies that address both variables simultaneously are scarce and necessary since they can explain the possible mechanisms of interaction linked to the etiopathogenesis of depressive disorders in this particular group since the literature suggests that psychological well-being could be a variable that promotes mental health. Based on the relationship documented in the literature between depression and physical health conditions, it is finally discussed how psychological well-being could potentially act as a protective factor against various medical diseases, and being able to guide effective therapeutic strategies focused mainly on the promotion and prevention in university students.

Keywords: *Depression, Students, University*

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Depressive Symptomatology and Depressive Disorders: Conceptual and Epidemiological Aspects

Depression is a highly prevalent mental disorder in our country and is currently considered a that obeys multiple causes, in whose etiology participate genetic, cerebral, environmental, characterological, and sociocultural factors(1). The rates of this mental disorder have been increasing in recent years, to the point that some authors speak of the " era of depression," as before it was that of anxiety, and, in Freud's time, the time of hysteria. The prevalence of depression in the general population can be estimated at between 9% and 20%, and, although only half or fewer end up receiving specialized care, depressive patients constitute between 20% and 25% of those who consult their general practitioner due to a psychiatric problem(2).

Since the time of Kraepelin and Kretschmer, clarifying the boundaries between "ordinary sadness" and clinical depression has been a

significant concern. Much of the controversy has centered around the question: What limit can be established on the continuum from the experience of sadness to the major depressive episode?[3].

In the last twenty years, there has been a drastic proliferation of psychological theories concerning the etiology of depression. Much of the empirical endorsement that supports the current psychological models of depression comes from studies conducted on sub-clinically depressed subjects with a depressed mood but not on more severely depressed patients, who are thus classified according to the score obtained in a given depression scale or inventory[2]. This methodological strategy supposes the implicit assumption of the so-called continuity hypothesis of depression, which conceives this disease as a continuum and thus, that any person could be located on it at any given point[4]

It is known that, in the most severe states within this continuum, the individual can threaten their life, which transforms depression into a life-threatening illness. In the world, suicide is among the top ten causes of death, and more than one million suicides are committed per year, 30% of which occur in university students[5]. In this sense, the question inevitably arises: what factors could explain that, within a group of people who no longer want to live, a third are young people who are just beginning to forge their future? Faced with this question, a brief review of studies that have addressed mental health in university students is presented below by investigating the prevalence of depressive symptoms and its relationship with different sociodemographic variables. In turn, an approach from the perspective of psychological well-being and the variables that promote mental health in the general population, including university students, is made.

Prevalence and sociodemographic aspects of depression in university students at an international level

The rates of depressive disorders reported in foreign universities are high[6, 7, 8, 9, 10, 11]. Research on the prevalence of depression in university students at the international level, incorporated in this review, includes countries such as Colombia[9, 12, 13], Peru[14, 15], Brazil[16, 17], Mexico (18), United States[19], Australia[20], and China[11, 21]. In general terms, it is observed, between 30% and 50% of university students from those countries show depressive symptoms, figures that are relevant and statistically significant *(Table 1)*. There are several studies on the prevalence of depressive disorders in university students, with different methodologies and sample sizes.

In addition to this, there are findings on suicidal behavior in young university students--which are worrisome--with annual rates that are between 18% and 41%[5, 12, 22, 23]. This year, an investigation was conducted at the Universidad Nacional de Ucayali, with a sample of 431 medical students, in which it was found that 42.3% presented a depressive picture, and of them, 15% showed levels of suicidal ideation of medium and high intensity[24]. Similarly, in 2017, in an investigation conducted in Brazil, with a sample of 637 students from the Universidad Federal de Mato Grosso, a presence of 9.9% of suicidal ideation was estimated during the 30 days prior to the research[16].

An interesting meta-analysis published in 2016 incorporates studies published between 1982 and 2015 that evaluated depression, depressive symptoms, and suicidal thoughts in undergraduate medical students. The study includes 43 countries from all continents, with a sample of 122,356 students. The findings show a 27.2% prevalence of depressive symptoms, 11.1% prevalence of suicidal

Table 1. Synthesis of studies on the prevalence of depressive symptoms in students at an international level.

Country	Sample	Prevalence
Colombia[12]	625 students of different majors	49.8%
Colombia[9]	218 students from the Pontificia Universidad Javeriana-Cali	30.3%
Colombia[13]	1344 Students of all majors at Universidad CES	47.2%
Perú[14]	382 Peruvian students	40%
Perú[15]	119 medical technology students Universidad Nacional Mayor de San Marcos	38.7%
Brazil[16]	637 students from Universidad Federal de Mato Grosso	41.9%
Brazil[17]	761 medical students	34.6% depressive symptoms 37.2 anxiety symptoms
Mexico[18]	8197 Baccalaureate and undergraduate students through CES	14.7%
United States[19]	1050 medical students University of California	5% depressive symptoms 11.5% some anxiety disorder
Australia[20]	800 students	39.5%
China[11]	5245 students of various majors	11.7%
China[21]	39 studies conducted between 1997 and 2015 32,694 Chinese students of various majors	23.8%
Meta-analysis 43 countries[25]	122,365 medical students from different universities	27.2%

ideation, and, among medical students who tested positive for depression, 15.7% sought psychiatric treatment[25].

The background described above can be analyzed in a more specific way by incorporating sociodemographic variables relevant to these studies: gender, age, socioeconomic level, and marital status, among others, showing differences between them and mixed results. For example, regarding the gender variable in a study conducted in Colombia, where 30.3% of the students reported depressive symptoms, a higher prevalence was observed in women[9]. For the socioeconomic stratum, it is evident an inverse ratio between the severity of the depressive symptoms and the socioeconomic stratum to which the young people belong, with more severe symptoms in the lower socioeconomic stratums.

In addition to these findings, Riveros,

Hernández & Rivera in the city of Lima, Peru, found that there were also differences in the intensity of depressive symptoms according to gender[6]. Depression manifests itself with greater intensity in women than in men: in women 15.35% (mild depression) and 2.30% (moderate depression), compared to 5.30% (mild depression) and 2.30 % (moderate depression) in men.

In Colombia, a study aimed at establishing the association between depression and academic performance in undergraduate students from the University of Magdalena, found a prevalence of depression of 38.5%--again higher in women (40.3%)--identifying, in addition, depression as a risk factor for adequate academic performance[26]. Another risk factor found was being over 20 years of age, which , according to the authors, could be explained because the presence of depression in adolescents is lower than in adults.

On the other hand, systematic reviews and meta-analyzes guide the evaluation of these results. A systematic review by Chen analyzed 24 articles that met the established inclusion criteria and found that the prevalence rates of depression reported in university students ranged from 10% to 85%, with a weighted average prevalence of 30.6%, which suggests that university students present rates of depression that are substantially higher than those found in the general population[11]. Within this review, sixteen articles reported gender differences. Most of them found a higher prevalence among women, six articles failed to detect any statistically significant gender difference, and one found that men had a higher rate of depression[11]. In the 16 studies that report gender differences, participants reported higher rates of depression, with a weighted mean of 29.6% compared to 24.9% in men. Regarding the year of study completed, higher prevalence rates were observed in the first years of study. This systematic review[11], such as the research conducted in Colombia[9], found that the socioeconomic determinants of prevalence indicate that higher family income lead to lower rates of depression.

Next, studies at the national level will be reviewed to analyze how these variables behave in this context.

Prevalence studies and sociodemographic aspects of depression in university students nationwide

According to Baader[27], the study of the prevalence of psychiatric pathology in Chile conducted by Vicente[28] shows that more than a third of the Chilean population would have had some psychiatric disorder throughout their life, while one out of every five has had a disorder in the last six months. With regard to the child and adolescent population of our country, the general prevalence of mental disorders reaches 22.5%, with disruptive behavior, anxiety, and affective disorders being the most common problems.

Depressive disorders at the national level are equivalent to the rates found at the Latin American level[28]. In national universities, the incidence of depression (about 16.4%) exceeds the rate for both the general population (15%) and equivalent age group (13.8%)[29].

Four national investigations stand out: one at the Universidad Austral[30], another at the Universidad de Concepción[31], a third investigation that includes a university in the metropolitan region, and another one in the IX region[32], where figures found a range from 13.7% to 28% of students with depressive disorders (Table 2). Regarding the relationship between the variables sex and depression, differences were observed in the three investigations, with women showing higher figures compared to men.

A fourth study about the prevalence of

Table 2. Synthesis of studies on the prevalence of depressive symptoms in students nationwide.

University	Sample	Prevalence
Universidad Austral[30]	804 students of various majors	13.7% major depression 26.9% depressive disorders
Universidad de Concepción[31]	632 students of various majors	16.4% depressive disorders
Universidad de la Región Metropolitana and Universidad de la IX Región[32]	580 students of various majors	28% depressive disorders
Different Chilean Universities[33]	460 students of various majors	22.8 % depressive disorders

psychopathology in university students in our country who attend a student health service, revealed that students present mood disorders in higher rates than the prevalence found in Chilean universities, (22.8% in depressive disorders) and with higher rates than that found for the equivalent age group and the general population. They found that the most incidental types of conditions correspond to single episodes of major depressive disorder, mood disorders under study, and dysthymia[33]. According to the authors, the evidence is consistent with national figures, in which major depression and dysthymia are the most prevalent disorders. On the other hand, no significant differences for mood disorders by gender were found, despite reports of a higher prevalence of depressive disorders in women. In any case, it should be noted that the studies at the national level are still incipient and that more evidence is required to establish conclusive results[33].

Changes in the national higher education system: A new student profile?

A relevant aspect to consider when analyzing the available data is the changes that the higher education system has experienced in our country in terms of its overcrowding and expansion, which have a direct impact on changes in environmental conditions and in the profile of the students--variables that may be significant when analyzing their mental health problems.

It should be noted that during 2009, the number of students enrolled in Chilean higher education exceeded 876,000 students, which today represents approximately 5% of the total population of Chile. The same year, a novel phenomenon was also observed: female enrollment in higher education surpassed male enrollment for the first time. These figures have been the result of a significant increase in enrollment, which has transpired over the last 30 years and has been shaping the state of Chilean higher education. This is consistent with the growing increase in the economic coverage of higher education students between 1990 and 2009, with respect to the total population in the range between 18 and 24 years of age[34].

For both universities and vocational colleges, there was an enrollment increase throughout the study period. The annual undergraduate growth rate was over 5.9% in the first decade and 7.5% in the second.

In this context of accelerated growth of the university population in recent years, the state has played a central role in supporting this significant expansion of the education sector through grants or loans for students, with the aim of achieving more equitable access to education for the different social sectors of the Chilean population. This expansion and massification of university education have generated an important change: the configuration of a new student profile. The new type of student no longer belongs only to the segments with the best academic performance of secondary education[35], does not come from privileged educational systems, and belongs to more vulnerable social groups; conditions that would eventually be associated with a greater risk of presenting mental health disorders in Latin American adults and adolescents, according to an extensive review of works published from 1982 to 2006[36].

Due to the increase in risk or vulnerability factors for the development of mental disorders, what elements could promote mental health in university students?

The Concept of Psychological Well-being

The current academic debate around wellness and health has been based on two ancient philosophical traditions: hedonism and eudaimonia. From the hedonic perspective, well-being is understood as the presence of positive affect and the absence of negative affect, while from the eudaimonic perspective, it is proposed that well-being is the consequence of a complete psychological functioning, which allows people to fully develop their personal potential[37]. Therefore, there is no single definition of well-being: concepts such as quality of life, happiness, absence of disease, satisfaction with life, and balance between positive and negative effects are widely used to approach the phenomenon. Faced with this plurality, well-being studies[38] classify the variety of concepts into two large categories: those aimed at obtaining a specific result that reflects the presence of positive affect and the absence of negative affect, related to the search for happiness (associated with the concept of subjective well-being) and those oriented to the study of personal development and growth, which rather aim to determine psychological well-being[39]. This concept, which has its bases in the eudaimonic tradition[38], arises from concepts proposed by humanistic psychology such as self-actualization[40] or self-realization[41], which have not had a significant impact on the study of psychological well-being, mainly due to the lack of reliability and validity in the procedures used for its measurement[42, 43, 44].

Looking for the points of convergence between all these formulations, Carol Ryff[45] suggested a multidimensional model of psychological well-being, with six dimensions linked to an optimal level of well-being. Each dimension poses a different challenge that people encounter in their effort to function positively[46, 47]. These dimensions, expressed on a measurement scale[45], are the following:

1. Self-acceptance: It is related to the fact that people can feel satisfied with themselves, being aware of their limitations.
2. Positive relationships: Ability to maintain stable and good quality social relationships; in other words, the ability to love and the development of mature affectivity are fundamental components of well-being and mental health.
3. Mastery of the environment: Personal ability to create or choose favorable environments for oneself, which generates a greater sense of control over the world and the perception of being able to influence the context.

4. Autonomy: Being able to sustain one's own individuality in different social contexts and in the face of social pressure, which favors self-regulation of behavior.
5. Life purpose: Have clear goals and be able to define objectives throughout the development of the life cycle.
6. Personal growth: It is the ability of the individual to create the conditions that allow them to develop their potential and continue to grow as a person.

Psychological well-being and Sociodemographic Variables

In order to understand the nature of psychological well-being based on this model, research has focused on evaluating general characteristics of the population and levels of psychological well-being[48]. For example, in relation to age, it has been observed that in people belonging to the elderly range, the six-dimensional model is not applicable in the same way as in younger people. In older adulthood, the factors associated with well-being seem to be more closely related to variables related to health and family affection[49]. The initial validation of the test, conducted by Ryff, compared the dimensions of psychological well-being in three significant age subgroups: young people (18-29 years), adults (30-64 years), and older adults (65 and over), finding differences in the dimensions: environmental mastery, autonomy, purpose in life, and personal growth. The first two dimensions showed increasing rates from a young age to middle adulthood, while life purpose and personal growth showed lower scores as they progressed from middle adulthood to older age. The dimensions of self-acceptance and positive relationships with others did not show relevant differences according to age groups[43].
The differences in relation to the gender and well-being variables have been reported by various studies[43, 47, 50, 51, 52, 53], which relate these differences according to different dimensions of the Ryff questionnaire. Thus, for example, Akther[51] observes that the scores on the psychological well-being scale among male and female Indian students differ significantly, presenting lower levels in the female population. Part of the discussion places the dimension positive relationships with others as an interesting phenomenon to investigate, as there is agreement in research that indicates this scale as the only one that is strongly related to the female gender. The study by Ryff and Keyes[47] indicates that only this dimension showed a significantly higher difference in women than in men, results in agreement with later studies conducted in Italian[54] and Chilean[32, 53] populations.
On the other hand, it is important to note that gender differences also vary by age group. A study by Visani et al.[50] with an adolescent population shows homogeneity in the scores between men and women at a general level. However, it is observed, mainly in women, that the scales of Environmental Domain, Autonomyor Positive Relationships with Others, perform a protective role against stress and future adversities, helping them reduce the risk of depression. In a Spanish study[52] with male and female populations of various age groups, significant differences were found in the dimensions of Self-acceptance and Autonomy: women obtained the lowest scores on these scales and, unlike other studies mentioned above, the authors observed that the dimensions. Positive Relationships with Others and Personal Growth were similar for both genres.
Thus, the gender variable in relation to well-being may be influenced by the age range. In relation to the interaction between age and sex, differences were observed in: Self-acceptance, Personal Growth, and Environmental Domain[52]. For

Self-acceptance, they observe significant differences between both sexes, being men who present higher scores; this difference would be accentuated as evolutionary development proceeds. Regarding Personal Growth, differences according to sex are observed, which increase as the age of the age group increases: in all stages, it is men who present the highest scores in this dimension. Finally, regarding the environment domain, it is observed that women obtain greater stability and for both sexes, and the highest scores on this scale are obtained in adulthood[52].

An Indian study[55], using the Ryff scale, explored the impact of demographic factors on the psychological well-being of 280 university students, including the gender variable, but also the educational level of the parents and family income. The findings did not identify gender differences in relation to psychological well-being; however, the parents' educational level and economic income were associated with differences since higher income and higher educational level significantly increase the levels of psychological well-being of their children who study. These findings would be consistent with the inverse relationship observed between the prevalence of depressive symptoms and socioeconomic and educational level, which suggests that depression and psychological well-being could be two conditions that are unevenly distributed in university students[56]

Psychological well-being and Depression in University Students

The stage of the life cycle in which most undergraduate university students find themselves is late adolescence, and it is precisely there when some mental health problems are triggered, which do not appear as frequently in previous stages of life--such as mood and anxiety disorders. As part of the challenges of this stage of the life cycle are the achievement of greater autonomy, assuming academic responsibilities, responding to personal and family expectations, developing sexual life and establishing couple relationships, consolidating personal identity, among others. This period of psychosocial moratorium that society offers to the young (based on the culture and subculture of belonging) prolongs adolescence, allowing the subject to progressively insert themselves into society. That is why the demands of study and improvement at some social levels contribute to extending this period[57].

The progress through the university represents for the student an experience of the life cycle that will define the rest of his life, with characteristics that are his own. The university environment constitutes a place in which the competencies and abilities are put into play to achieve the academic objectives within a certain period and students must face a significant number of changes in their vital circumstances, such as adapting to new teaching styles, economic difficulties, and significant amounts of uncertainty regarding the future[5]. Academic demands, difficulties in the development of learning, and the acquisition of skills pose situations of failure or success, accompanied by a new pace of study, hourly intensity, the demands of teachers, group pressures, competition among peers, changes in feeding schedules, and changes in the sleep-wake cycle, among others, which can have a significant impact on the health and psychological well-being of students[13]. All these challenges require the development of psychological functions such as the capacity for self-management and self-regulation[27]. Additionally, in some cases, entering the university requires leaving home, family, friends, and everyday surroundings, which causes a significant disruption of their support networks[58].

Fisher and Hood[59] showed that students experience a significant increase in levels of depression, obsessive symptoms, and loss of concentration after six weeks at university. Likewise, Mosley et al.[60] report in a study conducted on medical students that students experience higher levels of depression at higher levels of stress.

Based on the previous findings, various researchers worldwide have focused on studying well-being in this population[61, 62, 63], relating depression with low levels of psychological well-being. However, this is one of many ways of approaching the problem.

Denovan & Macaskill[63] conducted a study in the United Kingdom that addresses the stress of adaptation to university life from a Positive Psychology approach, to investigate the characteristics that facilitate adjustment during this process. By measuring subjective well-being in 192 students upon entering university and repeating the measurement six months later, they found that the variable optimism (related to well-being) mediates the relationship between stressors and adverse effects over time, helping students reduce the impact of stress on subjective well-being. The same phenomenon was observed in those students with high levels of self-efficacy. Thus, variables related to well-being could operate as protective factors against adversities and the environmental stressors in the university context.

Che Lin [64] studied the relationship between self-esteem, psychological well-being, and depression in a sample of 235 Taiwanese university students. The results show that psychological well-being is a mediator between self-esteem and depression; that is, well-being favors mental health by creating a positive basis for the reduction of mental health symptoms in general. This result is consistent with previous research reporting a positive correlation between self-esteem and psychological well-being[65]. It is possible then to hypothesize that psychological well-being operates as a proximal factor that protects people from depressive symptoms.

Psychological well-being and Depression in University Students: Two Independent or Dependent and Opposing Dimensions

Some authors have suggested that clinical depression is the loss of psychological well-being[66, 67]. In the midst of many theories, the Homeostasis Theory[66] is one of the few that specifies a control mechanism, stating that under stable living conditions, people maintain a fixed point or cognitive balance generally in the positive range. It has been argued that psychological well-being is based on relatively stable personality characteristics that maintain self-esteem due to an intrinsic control mechanism that is analogous to "homeostasis." When unfavorable events occur, psychological well-being is affected; however, this change is temporary until stable personality characteristics take over and ensure that well-being returns to the set point. Nevertheless, genetic predispositions and adverse life events can challenge this homeostatic mechanism by reducing levels of psychological well-being below their homeostatic range[66].

The relationships between mental health, well-being, and mental illness are complex, and people can experience very low levels of well-being even in the absence of overt mental health problems. This conceptual distinction is best exemplified in the model that suggests that mental illness and psychological well-being are related to different phenomena rather than being the counterpart within the same dimension[68]. This model maintains that mental illnesses and mental health are related but constitute different dimensions, although not

necessarily independent since they could have intersection points with each other. For example, people with a good level of psychological well-being and suffering from an episode of mental illness could show higher functioning (for example, fewer days lost from work and greater functional capacity) compared to those who have "moderate" levels of well-being[69]. If this last theoretical proposal is correct, what are the possible points of intersection between both dimensions?

Discussion: Potential relationships between depression, health, and psychological well-being.

The changes associated with university life can significantly affect the mental health of students, through a series of challenges inherent in a demanding academic context. Clinical disorders such as depression and anxiety have been widely studied, as could be seen in the present review, demonstrating their relationship with these factors. In the university environment, one of the main factors associated with depression is academic stress, which is constituted as a triggering element and, at the same time, as one of the maintenance factors of depression[13]. The new demands imply for the human being an adaptation process that can result in an initially adaptive stress response, but which, when sustained over time, could contribute to the development of various mental disorders.

On the other hand, the relationship between stress and depression is not only established from a clinical point of view, but also seems to have certain common mechanisms that establish an etiological and pathophysiological continuity between both phenomena, linked to brain neurochemical and neuroendocrine alterations of the HHA axis, even with a possible deterioration of the system, which would explain the frequent overlap of both entities in the clinic[70].

A novel proposal to approach the intersection of these phenomena is made by Slavich and Cole[71], who propose that the subjective perception of the social environment, for example, the perception of being socially isolated can generate changes at various levels of body systems, such as the central nervous system, the HHP axis, intracellular signals, and gene expression, and transcription factors. The authors call this causal mechanism "social signal transduction"[71]. For example, a study conducted by Murphy et al.[72] shows that perceived social rejection in adolescents is interpreted as a threat to their position in the social hierarchy, activating molecular mechanisms of phylogenetic origin to respond to potential physical aggression, causing increased production of inflammatory molecules (NF-kB and I-kB). It should be noted that this phylogenetic response can cause a potential increase in the risk of developing cardiovascular diseases and affective disorders in these individuals[73].

In this sense, a critical aspect of the role of psychological well-being in biology and health is that it seems to influence as a buffer or protector against the adverse effects of negative experiences[74]. For example, some studies in samples of older women have found that those with higher levels of purpose in life, more sense of personal growth, and better interpersonal relationships, had lower cardiovascular risk and better endocrine regulation, which is manifested in younger cortisol levels in saliva throughout the day[75]. This link between lower cortisol levels and eudaimonic well-being has also been proven in other studies[76]. Regarding inflammatory factors, people with better relationships with others (interpersonal well-being) and a sense of purpose in life show lower levels of IL-6 and its soluble receptor (IL-6r)[77].

A recent study shows that the same wellness dimensions (positive relationships with others and life purpose) turn out to be protective factors against depressive symptoms in university students[32].

Beyond the eventual neurophysiological consequences and for the body in general, the factors that threaten psychological well-being at this stage of the life cycle can lead to an accumulation of negative consequences for adult life through their impact on the development of the career and social relationships of the student. University-stage stress and depression have been linked to deficits in academic performance, instability in relationships, suicidal thoughts and attempts, and poorer job performance[78].

Based on the evidence, it is possible to affirm that depressive disorders in university students present a higher rate compared to the general population, which shows a reality of potential clinical relevance at the public health level. Thus, it is necessary to identify the intervention needs in a population that, given its idiosyncratic characteristics, constitutes a risk group for the development of various mental health problems. In this sense, the promotion and enhancement of psychological well-being could have a positive impact on the mental health of students, facilitating the deployment of timely interventions not only from a therapeutic approach but also from a perspective focused on prevention.

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Mood Disorders In Teleworking In The Context Of Covid-19

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ABSTRACT

Teleworking (TW) is a type of work established in the '70s in the United States due to the oil crisis. Chile has applied it legally since 2001, showing a 31% increase in its use since 2009 and up to 72% as of March 2020, due to the arrival of the Covid-19 pandemic and the subsequent decrease in social and workplace exposure suggested by health authorities to prevent contagion.

Although TW was already used in exceptional cases of the 45-hour workweek, in 2020, 72% of companies nationwide have teleworkers. It should be noted that in 2006, the leading technology companies reflected only 25% of the use of this form of work despite having this category, according to the Chilean Association of Information Technology Companies (ACTI).

The objective of this research is to determine whether TW develops mood disorders in the context of the Covid-19 pandemic. The review of articles and research related to teleworking with and without a pandemic context was used as the methodology for this paper.

Among the results obtained, the decrease in physical fatigue caused by commuting to work and more contact with family members were highlighted. However, this could be related to greater health and safety problems due to reduced office space, noise, insufficient healthy breaks, poor ergonomics, quality and mastery of technology, available connectivity, and the ambiguity of working or doing housework.

In conclusion, telework deserves greater attention, interest, and contribution of studies of mood changes that may manifest during its execution; even more so under the context of a pandemic and the sum of social, academic, and family changes experienced concurrently by teleworkers.

Keywords: *Telework, mood disorders, covid-19 pandemic*

INTRODUCTION

Compared to the results obtained in June 2019, teleworking in Chile has increased more than 100% as of March 2020 — just as Chile was entering phase 4 of the Covid-19 expansion, which led to strict sanitary measures. One of the measures that caused the greatest social impact was physical isolation based on staying at home, which led companies that had Information and Communication Technologies (ICT), which allowed them to conduct work activities virtually according to the definition of the International Labor Organization (ILO), to use telework.

However, it is not enough to address the usual changes that may occur when a face-to-face worker becomes a teleworker, but also to evaluate mood changes that may manifest themselves within the context of the pandemic in terms of the prolonged isolation at the social, work, and academic level of all family members and its emotional

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impact on the teleworker.

DEVELOPMENT

Definitions and use of telework in Chile

Teleworking emerged in the 70s as a result of the oil crisis in the United States. It was created by the physicist Jack Nilles, who is considered the Father of Teleworking for developing the following concept: "Teleworking is the possibility of sending work to the worker, instead of sending the worker to work"[1]. In this way, Nilles contributed to the development and improvement of society; however, the usefulness of this idea was considered years later.

The International Labor Organization (ILO) — to which Chile belongs since 1912 with 62 conventions, 51 of which are still in force[2] — defines teleworks as follows:

a) activity that is conducted in a location far from a central office or production facilities, separating the worker from personal contact with work colleagues who are in that office.

b) way of organizing and conducting remote work with the assistance of Information and Communication Technologies (ICT) at the worker's home or in places or establishments that do not belong to the employer, facilitating communication with technological support according to their needs[3].

In Chile, teleworking was recognized for the first time through the ruling of Law No. 19.759 in 2001, which incorporates it as a case of exception to the maximum duration of the ordinary 45-hours work week enshrined in article 22, paragraph 1 of the *Labor Code (= CdT)*[4]. However, though this was a choice for employees, it did not contemplate limits on call hours from their employers. That is why, on March 24, 2020, a law that regulates telework, with the "right to disconnection," which frees employees from responding to requests from their employer for a period of 12 hours, was published in Chile[5].

Although it is true that telework in Chile has been legally recognized since 2001, it was already in use in previous years. According to the report of the National Institute of Statistics (INE) of the Chilean labor department, a survey from 1997 to 2000 revealed an increase in home-working in the Metropolitan region, obtaining an increase in the main activities of workers, as well as activities by sex[6]. Even though this increase had been taking place over the years, the Chilean Association of Information Technology Companies (ACTI) showed in 2006 that only 25% of the companies that make up said association used teleworking, a figure considered very low for leading technological companies[7].

After the confirmation of the first case of Covid-19 in southern Chile on March 3, 2020, and the announcement of phase 4, the global HR and employment services consultancy Randstad Chile announced the use of teleworking in 72% of the companies surveyed, an increase in comparison to 31% obtained in June 2019. However, in both studies, the modalities of technological use were similar[8]. Likewise, the General Manager of the Cisco subsidiary, Gabriel Calgaro, mentioned that, in the second week of March 2020, 30,000 meetings with 60,000 connected users took place, and 24 hours later, it reached 37,000 meetings with 87,500 participants[8].

This increase in modality led to 52% of the employees reporting fear of losing their job in addition to feeling anxious and stressed. The application Workie Talkie conducted a survey between June 1-7, 2020, to 1560teleworkers in the context of the pandemic, asking questions such as, "How do you feel?", which showed the following results 18.6 % acknowledged

feeling stressed; 11.2% anxious; and 9.7% frustrated. Another 8.1% admitted feeling depressed, and 7.3% angry[9].

The pandemic has generated changes in the habits of family members; in this context, it is necessary to know more about mood disorders and mood changes that may occur in order to identify, anticipate, and stop the development of the symptoms that may generate in the teleworker.

What are mood disorders?

The set of mood disturbances among which depression, mania, and mixed states stand out are known as thymic disorders or mood disorders[10]. There are biological studies of heredity, biochemical aspects, the role of catecholamines, hormonal and psychosocial factors, and premorbid personality factors as etiological causes of mood disorders[11]. Anxiety disorders also affect mood[12]. Stress contributes to neuroendocrine, immunological, emotional, and behavioral processes and responses to situations that imply a demand for adaptation greater than usual for the body and/or are perceived by the individual as a threat or danger, either for their biological or psychological well-being. The threat can be objective or subjective, as well as acute or chronic. In the case of psychological stress, what is crucial is the cognitive component of the subject's appreciation of the situation[13].

Furthermore, numerous epidemiological studies have confirmed Kraepelin's observation that stressful events are more frequent before the first depressive episode. In the case of personality types, there is a greater predisposition to mood swings such as depression in dependent, obsessive-compulsive or hysterical personalities[11]. This is also confirmed by the Director of the Postgraduate School in Severe Personality Disorders of the University of Valparaíso, Roberto Castillo, in an interview conducted by telephone. However, the articles found in relation to teleworking before and during the Covid-19 pandemic are not directed towards the study of mood disorders but rather to what is discussed next.

In accordance to the study published in May 2020 by the journal of *Sustainability " about telework in the context of the Covid-19 pandemic,* it was concluded that telework should be seen as a multidimensional phenomenon rather than a simple absence from the office to which the majority of public and private organizations have resorted without precedent. Therefore, it can be considered that the call to telework is forced by the circumstances of the spread of Covid-19; in this context, the company forces employees to adopt teleworking as a way to continue their employment relationship, as it was evidenced that no company had contingency plans specifically designed to resolve emergency situations such as the current pandemic[14].

Its authors, Standen, Daniels, and Lamond, cite nine benefits of TW provided by Warren in 1987, such as autonomy for decision-making, opportunity to develop skills, freedom to fulfill responsibilities, obtain goals, and choose ideal conditions for the development of TW. They note that while Warren provides a sound basis for studies of TW at home, the well-being of each and their relationship to each other has not yet been examined in detail.

Additionally, they cite that work and family life are clearly more susceptible to intrusions when they are conducted in the same place, causing a cognitive or emotional disconnection. The findings of this study concluded that the teleworkers present more emotional changes than office workers, which invites stress management to be directed at teleworkers rather than office workers[15].

On the other hand, in 2019, the Journal of Happiness Studies evaluated the subjective well-being of teleworkers, found that telework reduces mobilization fatigue

but increases stress for both men and women due to the pressure to perform and meet the expectations of the employer and their own expectations, so this review suggests that the benefits of teleworking for employees be reconsidered, and, that to improve the quality of life, the government or employers should provide more support to homeworkers, such as childcare, parenting the elderly, physical support such as enough space to work, and a social network that can support homework practices. These supports would enable home-based workers to better deal with loneliness, stress, and conflict between work and family, and would help them develop boundaries in time and space between the worlds of home and work to maintain higher levels of self-motivation. It also asks to regulate long working hours to promote an adequate balance between work and life, thus maintaining a harmonious family relationship[16]. It was also revealed that people who perform telework and deal with work-home conflict and role ambiguity at home negatively influence the intention to continue teleworking among teleworkers[17].

The Journal of Applied Psychology, in 2007, published a meta-analysis where they reviewed published studies from magazines, book articles, and also unpublished studies in the areas of administration, psychology, education, sociology, and engineering, and they evaluated the good, the bad, and the unknown of teleworking. In this study, they found that the teleworking contributes to positive effects due to a perception of autonomy, which was favorable for the teleworker's performance, in addition to showing reduction of stress and resignations[18].

Human capital consultants of Fundación Chile, in their Engagement and Teleworking survey in Covid-19 context based on a simple random sample in the form of an open and freely shared survey of people who were teleworking, surveyed 522 people and measured work engagement and burnout. These results were compared with benchmark results from Chile 2019.

The engagement results obtained showed a decrease of 0.714% for vigor, 0.35% for dedication, and 0.28% for absorption. These three measures showed higher percentages in the questions "When I get up in the morning, do I feel like working?", "Am I proud of the work I do?" and "When I am working, do I lose track of time?"

Exhaustion increased by 0.145% from 2019 to 2020, which is greater than the benchmark in 2019. Extreme state of wear reached 21% vs 28% in 2020. Among the benefits, the results indicated that the time that was previously used for commuting is now used for more time with the family; among the difficulties, an increase in chores at home was revealed.

When asked, "Do you feel that it has negatively affected you in any of the following areas?", multiple choice answers revealed results of 54% for the ability to concentrate, 45% for distress and loneliness, and 43% for mental health. Regarding home space where the TW is conducted, the survey showed that 36% use the dining room, 24% the study room, 15% the living room, while 11% use the bedroom and 10% improvise a room.

The conclusion in this survey shows an alarming low level of engagement and a high level of exhaustion, compared to the benchmarks in 2019[19].

CONCLUSIONS

Although it is true that we still do not have studies performed under the approach of mood changes with teleworking, it is essential to highlight that in the current context, due to the Covid-19 pandemic, the circumstances of the use of TW are not the same as in previous years.

The pandemic offers us a different view,

as not only is the teleworker at home, but also all the other family members, which requires more technological equipment and better internet connection services.

Teleworking parents that are with school-aged children who need their support for their tele-education demand the use of workhours to render that help, which causes self-abuse as it extends work hours, thus neglecting adequate, necessary, and healthy work breaks.

It is also important to consider the impact that can be generated at the mental health level of each individual by the restriction of outings, trips and social interaction that were used to counteract stress.

Let us remember that, currently, this work modality was not chosen but rather imposed by health authorities in order to avoid the spread of Covid-19 in the face of a health emergency experienced worldwide.

Clearly, these measures were necessary, but they deserve greater vigilance and research, mostly due to the prolonged isolation that this implied in teleworkers. Therefore, I suggest researching and learning more about this subject to confirm or rule out that this context causes mood disorders. I also suggest researching whether the patient has a prior history of mood changes and/or presents low or no capacity for adaptive flexibility based on their personality type

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Depression and Psychological Treatments: Who are the expert voices?

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ABSTRACT

Introduction: Depression is one of the most prevalent diseases among the adult population in Chile, being part of the Explicit Health Guarantees in our country. Their care involves psychiatric and psychological approaches with high costs for the public sector, which do not always manage to ensure the effectiveness of the treatment.
Method: A literature review to document studies on the perspective or opinion of patients undergoing treatment for depressive symptoms. Results: Various sources indicate the benefits of integrating the patient's perspective into treatment, with higher success rates compared to traditional intervention models.
Conclusions: We highlight the role of the patient and their experiences as one of the fundamental pillars of successful treatment. With this, efforts aimed at improving the coverage and effectiveness of treatment plans for depression would be favored by considering the formulation of clinical models or guidelines where the voice of the patient and their needs are recognized.

Keywords: *Depressive Disorder, Treatment Outcome, Patient Involvement, Primary Health Care.*

Depression in Chile and its Treatment

Depression is a disease of multifactorial origin, with a heterogeneous clinical presentation, characterized by the degree of dysfunction it may cause and the high social cost involved[1]. Depression is also one of the most common public health problems and with the highest burden of disease-associated worldwide[2]. In Chile, almost a third of the population has had a psychiatric disorder throughout their lives, with a 22.2% incidence during the last 12 months. Within this group, depression appears as one of the illnesses with the most significant presence in the adult population, with a life span incidence of 9.2% and 5.7% within the last year[3]. Similarly, the Pan American Health Organization (PAHO) indicates that the prevalence of depressive symptoms in the Chilean population is 15.8%, with a more significant presence in lower-income sectors and particularly among women[4], with figures doubling for the latter group[1].

Primary healthcare services (PHC) in our country have reported a life span prevalence of major depression of 23.6% and 10.9% during the last year[5]. Within this group, 42.2% of patients present some comorbidity with chronic illnesses[6].

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Depression, along with generating high costs to the health system, also involves significant psychosocial deterioration, being one of the most frequent GES (Explicit Guarantees in Health) benefits[7]. The public system offers coverage to around 70% of the population, especially to greater vulnerability areas, senior citizens, and a greater burden of illnesses[8, 9].

In our country, one of the numerous efforts to increase the coverage of the system is the development of specific clinical guidelines, which establish directives for the approach and treatment of both pharmacological and psychotherapeutic aspects[7, 10]. In the case of depression, these guidelines propose a care model characterized by being the first line of intervention in the primary care setting. The objective of this model is to be decisive in as many cases as possible and to promote collaborative work as part of a high-demand level of care that not always manages to provide timely coverage to all cases[10, 11].

As part of the professional work, any treatment for depression starts with a physician's screening (not a specialist), who, according to the symptomatic intensity of the patient, prescribes drugs and refers to a psychologist from the CESFAM (Family Health Center), or refers to COSAM (Mental Health Clinic), the latter being a more specific level of secondary care[7, 10]. This is how most clinical interventions in the public system are based on international guidelines aimed at managing the symptoms of depression, where the intervention's success is understood as the attenuation of depressive symptoms and the return to activities usual.

Nevertheless, in the national depression program, there would be some difficulties at the PHC level in detecting depressive disorders and their severity. It has been observed that this is associated with an increased risk of non-response to treatment, chronic or recurrent clinical pictures, and more significant functional disability[12]. Seeking to address these difficulties, it is necessary to explore and evaluate other aspects of the treatment that could influence their effectiveness, which is also a new contribution to current clinical models and guidelines.

The Patient's View

From the patients' perspective, it is possible to find various aspects that are not always considered when proposing treatments, which usually arise from scientific studies and the clinical opinion of experts[13]. This seeks to relieve the patients' perspective and experience, who can offer a different approach to the study of the treatments they themselves receive. Especially when this perspective seems not to be fully covered in the expert planning of the clinical guidelines, which also do not clearly indicate which intervention is more convenient in each case[13].

Ignoring the patient's opinion often results in cases that do not receive the minimum care required; they tend not to improve, have more relapses, and increase costs for the health system, not only in economic but also psychosocial terms[14]. This adds value to the patient's expertise regarding their experience of the illness, especially when discussing and planning healthcare policies.

Indeed, scientific evidence does not always translate into therapeutic success. The same happens with the feeling of well-being and improvement of patients. A systematic review shows how different studies converge on what some of the problems that patients encounter in their treatment for depression are: little continuity in the sessions, difficulty to feel interpreted by the clinical guide, scant communications with caregivers, and confusion in interventions that often follow contradictory indications[13].

Other reviews have also observed that

patients often reject interventions due to unfavorable attitudes towards drug use or involvement in psychotherapeutic processes[15]. Consequentially, ignoring the preferences and opinions of the patient could affect, for example, adherence to treatment and its success (16). Moreover, including patients in decision-making has been shown to significantly improve their treatment outcomes[17].

A study on the abandonment of depression treatment in primary care in Chile, from the perspective of patients, raises as central aspects of desertion: beliefs about depression as a disease, dissatisfaction with psychological care, negative perception of pharmacological treatment, low availability of hours in the healthcare center, interruption of care in the healthcare center, difficulties in attending the healthcare center, perception of improvement, and forgetting appointments[18]. The authors propose the latter as an indicator of low perception of need or relevance of the treatment. It is also important to note that, in this study, most of the people interviewed did not consult in the first instance due to a depressed mood. All the above, in addition to the difficulties in understanding the treatment received and its consequences, make it even more challenging to make sense of the process as something necessary and important.

Similar studies in our country indicate that many of the problems described by patients are the difficulty of access, infrequent sessions, lack of caregiver continuity, very short sessions, insufficient attention to personal problems, and excessive interest in knowing the symptoms[11, 19]. Additionally, the perception of little flexibility in the allocation of care hours and long waiting times become substantial barriers to treatment access[1]. In this context, many times, the assessment that patients make of their treatment does not always coincide with that of their caregivers, who tend to place emphasis on following indications rather than addressing the problems that the patient experiences. This is characteristic of the symptomatic medical model that does not contemplate a motivational perspective in the treatment of the patient[20].

Different studies show how patients who participate in decisions about their treatments become more involved in self-care awareness and are more empowered in their recovery[15, 17]. Likewise, patient groups often appear as a support network for people with pathologies that, from a medical-professional perspective, do not achieve good adherence to conventional treatments, including depressive disorders[21, 22, 23].

In the case of depression, several successful experiences with approaches that integrate the patient's perspective during their preparation and implementation have been described worldwide. This adds a realistic look to the therapeutic work that considers the patient's "expertise" in formulating the problem and the solutions offered[24, 25]On the other hand, the attitudes and behaviors of doctors and health professionals also contribute to adherence and patient satisfaction, especially the concern to communicate the indications for treatment effectively[18].

Communication and dialogue between professionals and patients: Listening to all voices

When a fluid dialogue between the treating team and the patients is achieved, better results are usually obtained. This is reflected in a decrease of symptoms and the strengthening of interpersonal relationships and the feeling of well-being. Positive communication is the first element of effective treatment[26, 27]. On the other hand, the optimism of both the patient and caregiver and the initial reduction of symptoms are fundamental conditions for a successful treatment. However,

when the health system is confusing, the caregivers are distant and fail to establish a sincere and empathetic dialogue with the patient, and the treatments show a marked tendency to fail[28].

Since the last century, it has been documented that the attributes that most favored collaborative work between patients and therapists for depression have been: a) the copying of problem-solving stress (modeling), b) own adjustments of the therapeutic relationship (feeling), c) social support of feeling helped, and d) closeness attributes of the therapist (treatment, gestures, and genuine attention)[29]. These aspects often arise from the dialogue with patients after their therapies and not as strategies or objectives previously defined as part of the treatment. In this line, positively valued post-treatment aspects are the closeness of the therapist, concern, time, and disposition[30, 31]. On the other hand, among the aspects most criticized by patients are the differences in perspective between professionals of the treating team, biases against the use of drugs over psychotherapy (or vice-versa), the feeling of not being heard, and of receiving standard treatment that does not suit their needs[32].

Final Discussion: Uniting Expertise

The various causes of mental health problems and mental disorders extend beyond individual characteristics (such as the ability to manage thoughts, emotions, behaviors, and interactions with others), including also social, cultural, economic, political, and improvement[33]. Therefore, mental health interventions should be capable of incorporating the complexity of each case to design more effective and relevant interventions. In this task, those who best know the intricacies of contextual realities are the patients themselves.

All of this should lead us to admit the importance of listening to multiple experiences and voices when making decisions. It is important that the experiences of all those involved are understood when conceptualizing the disease and defining its therapeutic approach. However, in this process, the patient's voice is usually not sufficiently heard. This, despite evidence that shows how active patient participation and dialogue are elements that often favor the success of treatments. The foregoing also contributes to psychotherapy, which is part of the treatment offered for depression, establishing a better connection between patient and therapist, opening the way to intervention models closer to motivational and participatory, moving away from the rigid perspective and protocols that are often promoted by clinical guidelines. Although the latter are tools that have proven to be useful for deciding courses of action at the level of public health policies, they do not ensure the success of any treatment, so looking for new contributions that help improve the user experience of the system audience will always be valuable. This essay intends to remind and rescue the importance of the personal experience of those who suffer from disease when treating it[20].

There are multiple therapeutic offerings for the treatment of depression. In all of them, the doctor-patient relationship is key to the success of the therapy, as is the communication between professionals on the treating team. With the above, it is reasonable to maintain that, based on good treatment for depression, it is essential to install a holistic understanding of the disease, understanding not only its physical but also socio-emotional components, recognizing the patient's voice as another pillar in the treatment of depression.

This proposal is accompanied by a series of challenges, among which are integrating the opinion of patients in the preparation of treatment plans, in addition to improving the training and education of therapists as

part of the transition to a more complex model, but also more complete.

Finally, as health professionals, it is essential to stay vigilant about the way in which the population and its needs evolve over time, along with understanding that treatments not only require adapting to the possibilities of the system but also to the needs of people.

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Analysis of a Bipolar Affective Disorder and COVID-19 Clinical Case from a Phenomenological Approach

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ABSTRACT

Introduction: the new disease called COVID-19, which emerged at the end of 2019 in China, and its consequences, such as social impact, grief, and the stress that it has generated, have become stressors that generate acute psychiatric pathology. An attempt is made to show, in a clinical case, how these factors are as important as the morbidity and mortality of the virus itself.

Method: Through semi-structured clinical interviews, with a phenomenological approach, data was collected. Then, a medical history presenting the case of a patient with a history of bipolarity who had SARS due to COVID-19 was prepared.

Conclusions: Although the evidence of the development of post-COVID-19 psychiatric pathology is still scarce, it is possible to infer that it significantly affects the future lifestyle of the person who experiences it, as it may generate feelings of anguish, fear, or anger, as well as post-traumatic symptoms. The use of a phenomenological research methodology opens the possibility of individually understanding phenomena from the unique perspective of the individual who experiences them.

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INTRODUCTION

Generalities:

In December 2019, a new beta coronavirus appeared in the city of Wuhan, Hubei province, China, causing a new severe acute respiratory syndrome (SARS), different from those known. In January 2020, the World Health Organization (WHO) gave it the name of SARS-CoV-2. Because of the vertiginous expansion that occurred in the following weeks in many countries of the world, WHO called the clinical expression of the disease coronavirus 2019 (COVID-19) and declared that the disease caused by SARS-CoV-2 was a pandemic on March 11, 2020[1].

At the time of writing, more than 16 million positive cases have been reported in 218 countries at the end of July, and it is estimated that more than 656,000 people have died[2]. Two other epidemic outbreaks of coronavirus have already been reported in this century, SARS-CoV in 2003 and MERS-CoV in 2012. From here, we can extrapolate a large part of the epidemiological evidence and the impact it subsequently caused from a psychiatric point of view[3].

COVID-19 Clinic and Psychiatry

Although there are practically asymptomatic forms, in some cases, COVID-19 can progress to severe respiratory syndromes

with high lethality. It can also infect other organs during the disease, including the nervous system, the latter being postulated to be a cause of neuropsychiatric manifestations.[4] The evidence of neuropsychiatric manifestations in patients with COVID-19 is still emerging, and the etiology of the psychiatric consequences is likely multifactorial. It is suggested that, in the context of an acute or subsequent viral infection, various types of neuropsychiatric syndromes may appear that affect the cognitive, affective, behavioral, and perceptual domains[5-6] and are expressed as insomnia, anxiety, depression, mania, psychosis, suicidal tendencies, and delirium[7].

A Lancet meta-analysis identifies a higher incidence of depression, anxiety, and post-traumatic stress disorder after the onset of the illness[8]. While social support is the main protective factor linked to the prevention of these disorders, there is consistent evidence showing that social isolation and loneliness are linked to worse mental health outcomes[9].

COVID-19 and Mood Disorders

The rapid spread of COVID-19, in addition to the implementation of preventive measures such as social distancing and isolation, its indirect consequences such as increased unemployment and the economic impact and people's concern for the evolution of their disease, social stigma, and traumatic memories, are potential generators of psychiatric pathology. People with psychiatric illnesses can be affected by the pandemic directly (contagion) and indirectly (social impact), which is why an increase in acute crises and exacerbations of psychotic and affective disorders is expected in the short term[10].

In patients with bipolar illness, it is crucial to consider the degree and duration of social isolation and the limited physical space in which isolation occurs because they can be associated with a wide range of adverse psychological effects, which include depression, decreased self-esteem, impotence, and anxiety. Some of these emotional disturbances will go away, but some people may also show late effects in the form of anxiety and mood disorders10. Overexposure to news media adds further stress while social distancing measures reduce opportunities for exercise, exposure to sunlight, participation in meaningful activities, and social engagement. Isolation can also affect zeitgebers that help keep sleep and physical activity stable. Possible adverse psychiatric effects and interactions of Hydroxychloroquine, the primary drug used in patients with COVID-19, should also be considered, including psychosis, mood swings, mania, and suicidal ideation as potential crisis-generating factors[11].

In this qualitative study, we review a case of a patient with bipolar disorder diagnosis who develops post-traumatic symptoms secondary to both morbid and social exposure to the virus. In order to add more information concerning how they are affecting our patients, this study aims to identify the degree of psychological affectation it can be unleashed (psychological consequences). It was conducted with a phenomenological approach to describe the events experienced more precisely.

Phenomenology and Psychiatry

Phenomenology is directed to the study of the lived experience regarding a disease or circumstance by the protagonist of the experience and seeks to describe the meanings of the phenomena experienced by individuals through the analysis of their descriptions. In the same way, it emphasizes reflective intuition to describe the experience as it is lived from his/her point of view, all the distinctions of our experience must be devoid of presuppositions and prejudices; instead, the theoretical foundations must be sought

to create a secure basis for describing the experience[12].

Heidegger specifies that phenomenology emphasizes the science of phenomena; this consists of "allowing to see what is shown, as it shows itself and insofar as it shows itself"; consequently, it is an objective phenomenon, therefore real and at the same time scientific[13]. In simple terms, phenomenology can be defined as a research approach that seeks to describe the essence of a phenomenon by exploring it from the perspective of those who have experienced it[14].

The phenomenological research approach arises as a response to the radicalism of the objectifiable. It is based on the study of life experiences, regarding an event, from the subject's perspective. This approach assumes the analysis of the most complex aspects of human life, of what is beyond the quantifiable. According to Husserl, it is a paradigm that tries to explain the nature of things, the essence, and the veracity of phenomena. The objective that it pursues is the understanding of the experience lived in its complexity; this understanding, in turn, seeks awareness and meanings around the phenomenon[15].

METHOD

In this study, a phenomenological approach was implemented to describe a clinical case and to emphasize the relevant aspects of the dialogic interview and reflect as faithfully as possible the reality of the world as it is for the patient.

The data were collected by direct interview of the patient during 4 semi-structured interviews of 1 hour with an interval of 7 days between each one. Open questions were asked so that the interview was partially guided, giving the possibility of answers that give the patient space to express what she had experienced in her own words. These began in June 2020, once the patient was discharged from the general hospital.

CLINICAL CASE

51-year-old woman, married with three daughters, housewife and diagnosed 15 years ago with bipolar disease, with a course characterized by a predominance of depressive episodes throughout her life. She lives in a coastal town at her home with eleven other people, who together constitute an extended two-parent family and is also a caregiver for her 87-year-old bedridden father. She was referred for admission and controls to the Mood Disorders Unit, which takes place in June 2020.

In May 2020, COVID-19 was diagnosed after being in close contact with her son-in-law with whom she lives and who had recently been in Santiago. Initially, the news is greeted with shock and disbelief, followed by concern primarily for the health of her older father and 1-year-old granddaughter. They were one of the first reported cases, so the news spread quickly, being criticized by her neighbors and judged for being infected. In the story, she constantly refers to the memory of the ridicule they were subjected to, of mistreatment by social networks where they were branded as dirty and irresponsible, intense feelings of anger, shame, and guilt appearing, but also of disappointment when feeling devalued by them. Days later, she went to the emergency room due to increased symptoms with chest pain, dyspnea, and fever. Multifocal Pneumonia was diagnosed for which she is hospitalized for management according to the local coronavirus protocol. From the hospital period, she remembers the feeling of loneliness since visitors were not allowed, that her only means of connection with the outside world was the mobile phone and that she spent much of the day (and night) thinking about

the sadness and guilt she felt for finding herself in that situation. On the third day of hospitalization, she presented rapid clinical deterioration, developing an intense fear of dying, feelings of insecurity, and anguish. She was transferred to the ICU due to respiratory failure and required invasive mechanical ventilation for 15 days. Once stable, she was transferred to medicine, where she spent 37 days hospitalized until she was in discharge conditions. At the end of this period, the need arises for the health team to inform her that while she was on mechanical ventilation, her father died as a result of COVID-19. Upon receiving the news, she said she suspected that something was wrong due to the evasive responses she regularly received from the family-focused on her improvement and not on providing information. Added to the initial sadness appeared a feeling of tranquility and resignation. During the weeks after hospitalization, feelings of anguish appear reflected in constant restlessness, anticipatory anxiety, and sadness, avoidance behaviors of everyday situations such as going out to the street or traveling by vehicle. She feels intense fear of being ridiculed or criticized by her neighbors or acquaintances again. She says that while she can go out, she prefers not to. She has frequent nightmares about it, as well as about the procedures that were performed, mainly describing the fear of general anesthesia as a potential generator of death. She also vividly remembers the fear she felt before hospitalization for her father's health, and feelings of guilt and regret appear because her grief is seen as an incomplete ritual due to the fact that she has not been able to visit his grave in the cemetery due to the COVID-19. After hospitalization, recurrent intrusive thoughts continued, with a significant deterioration in the quality of sleep and quality of life. She feels that the days are gray ("It seems like life loses color") and longer ("Instead of going, one just goes along"). As the days go by, a progressive melancholic tone stands out, associated with asthenia, adynamia, anticipatory anxiety, hypervigilance, and sadness with a tendency to easy and persistent crying. In her appearance, what stands out the most is the development of diffuse alopecia that has worsened over the weeks. She is not using makeup. The tone of voice is low, and the speech at times monotonous. The discourse is about self-improvement, a characteristic under which she defines herself: she has always been the one who has taken care of others, and it seems very strange that now the roles are reversed, and she has to allow others to take care of her.

DISCUSSION

In the intersubjective experience of the encounter between therapist and patient, the phenomenological method makes a distinction regarding corporeality, spatiality, temporality, and affectivity[16].

In relation to corporeality, it recognizes a lived body, the body that I am (Leib), which constitutes a pre-logical relationship between the subject and his body, lived in an immediate manner through movements and perceptions. However, also in the expression 'I have a body', the object body is put into play, the one that distances myself from me when I feel fatigue, discomfort, illness; a body full of meaning, prior to any dualistic abstraction of psyche-soma[17]. When approaching the present case from a phenomenological perspective, corporeality acquires a vital role. Pathological deviations are particular ways of structuring one's presence in the world: her face without makeup reveals a facial expression of sadness and fatigue, which she modifies with the content of the story, revealing displeasure and fear in relation to being in open spaces. Her body posture is continuously changing with

complementary gestures and continuous discreet movement in the hands and legs that suggest anxiety.

For phenomenology, our being-in-the-world always occurs in certain temples or states of mind which open the world to us before any cognitive act, and which are not mere subjective states that would only say something about ourselves but open us to the world prior to any cognitive act. It is because Dasein is already existing, inhabiting a world, that these can be presented as painful, pleasant, and, in return, feel scared or happy[18]. The affectivity of the story has an impact in such a way that both the tonality and cadence of the speech, as well as the modulation and gestures, recall the events suffered loaded with a powerful affective tone. Essentially it transmits the anger, sadness, and resignation of the different moments lived. Heidegger, in his [19]27 work Being and Time, highlights the importance of feelings as the essence of Dasein (which indicates the area in which the opening of the person towards Being occurs), and that, thanks to them, it is that being human acquires the essential characteristic of humanity19.

Temporality in phenomenological research becomes a coordinate that is given maximum importance.[20]Reference is made to another time, which does justice to human experience; the time lived, which cannot be measured, which is only expressible by metaphors or stories of concrete situations, "is the time lived by each subject from their own individuality, their personal and non-transferable experience, which makes their occurrence and their alterations are singular and unique in each person"[21]. This characteristic becomes evident in the case presented since the temporality is perceived in a lengthening of lived time, devoid of emotion and tends to monotony. Likewise, it must be remembered that temporality is an ontological character of Dasein and a condition of possibility of all knowledge, opinion, and objectification of time21. In this case, she keeps intact her ability to thematize the events of his biography, but she has profoundly changed "the time lived" in her subjective horizon; it is that way of living time that loses its intentional unity and its articulation in the context of past, present, and future"[22].

Of the conflicts in this case, we must mention that the COVID-19 epidemic has caused havoc throughout the world due to the morbidity and mortality it produces, especially in the elderly and people with underlying conditions that make them vulnerable to the most severe forms of this disease. But its consequences have not only been defined by its epidemiological impact, as there are other variables that contribute to a high-stress load.

There are studies that have shown that, as well as losing one's physical life, the loss of role, of social identity and of social networks, and social exclusion, loss of citizenship, economic capital, and access to resources are equally key in generating a problematic grief. However, although people can experience more than one of these losses simultaneously, the extent of their losses varies according to individual circumstances, when a person has experienced an extreme and profound loss, the type of coping skills, the psychological defenses used by the subject, and the social support available to predict the response to this situation[23].

Studies have shown that social support plays a critical role in psychological rehabilitation under the stress of an outbrake16. In the case described, one of the leading crisis triggers was social stigma. It has been said that when societies are under stress, social stigma appears with an emphasis that falls on people associated with high-risk groups, as well as on anyone considered "different" or potentially contagious, as it has happened to some ethnic groups at the beginning

of the pandemic[24]. If we consider that psychiatric illnesses are already prone to stigmatization, combining two stigmatizing pathologies, such as COVID-19, is likely to provoke negative feelings rather than support, leaving the person even more isolated.

One of the elements that make this case a therapeutic challenge is the presence of recent grief. Among all the specific situations of this disease, death from COVID-19 is the most feared of its consequences, not only due to physical death but also because of the social death that it involves. We have witnessed the abrupt decrease in in-hospital accompaniment, as well as family and social accompaniment at funerals, and we realize that death in solitude not only causes suffering for those who experience it, but it can leave sequelae in the form of grief for those who are close to them[23]. In any of the cases, it is perceived with pain and suffering, fear or hopelessness, which lead us to remove the subject from our daily thoughts; we avoid him or her and prefer to stay away from that single certainty. It is expected that, considering the defensive mechanisms of the patient and the support network she has, through psychotherapeutic intervention, she can achieve stabilization in the medium term.

CONCLUSIONS

As the COVID-19 epidemic continues to spread, we can say that there are already direct consequences on the mental health of the population, especially on patients with a history of psychiatric pathology.

The indirect consequences of COVID-19, including social exclusion, grief, social stigma, economic repercussions, among others, described in this case, seem to be even more traumatic consequences than the disease itself, as well as triggers of acute psychopathology.

The phenomenological perspective in the clinic allows a greater understanding of concrete existence. Also, it allows conceiving the disease as "a new way of being in the world," creates opportunities to learn from others' experiences, and has a broader and more in-depth understanding of the psychology of patients with mood disorders[15]. Thus, in the words of Oyarzun, the setting is placed for an "Encounter with the other", an other who is not me, who is suffering and who gives us the possibility of treating and providing psychotherapeutic support for the "who," and not for the disease or the "what," and to understand the depth of their experience[25], since normality defined as such becomes subjective when experiencing a similar stimulus, as in this case the COVID-19 disease.

Karl Jaspers said that "borderline experiences" are those that lead to philosophical reflection: death, loneliness, pain, anguish, melancholy. Without those experiences that blur that tiny picture in which we inhabit, there would hardly be any philosophical reflection[26]The reflection that we can make about the coronavirus has to do with the changes we will face. It forces us to restructure our "normality" and to observe with a new, more reflective look on aspects of how we deal with stress as a society.

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1. All works sent to the editors of the Journal of Mood Disorders, including all supplementary material, must abide by the following rules, prepared considering the style and nature of the Journal and the "Uniform Requirements for the Manuscripts submitted to Biomedical Journals "established by the International Committee of Medical Journal Editors, updated in October, 2001 (www.icmje.org). Additional editorial information may be found on the World Association of Medical Editors' website at www.wame.org.

2. Works must be original and unpublished, written in Spanish or English, and conform to the publication rules of the Journal. The works that satisfy the formal requirements will be submitted to the editorial committee. The Journal reserves the right to make modifications to the original texts.

3. All material must be sent via email and in Microsoft Word files for PC. Authors are required to keep a copy of the paper and of the email sent. The work must be submitted in the following format: page number on the top right corner, beginning with the title page, without headings, double-spaced, in letter size paper, Times New Roman 12-point font, flush-left. Text length is limited depending on the type of paper: Revision of articles, 25 pages max; Research papers, 20 pages max; clinical cases, 10 pages max (including up to 2 tables and 2 figures); and no more than 80 references. Letters to the Editor and brief reports must not exceed the 3 pages, including up to 6 references and 1 table or figure.

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Angst J. Bipolarity from ancient to modern times: conception, birth and rebirth. J Affect Disord 2001; 67: 3-19

Akiskal HS, Hantouche EG, Allilaire JF, Sechter D, Bourgeois ML, Azorin JM, et al. Validating antidepressant-associated hypomania (bipolar III): a systematic comparison with spontaneous hypomania (bipolar II). J Affect Disord 2003; 73: 65-74.

b. Organization as author

The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-284

c. Volume with supplement

Diekstra REW. Suicide and the attempted suicide: An international perspective. Acta Psychiatr Scand 1989;40 Supl 354: 1-24

d. Number of pages with Roman numerals

Fisher GA, Sikic BI. Drug resistance in clinical oncology and hematology. Introduction. Hematol Oncol Clin North Am 1995; 9:xi-xii.

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a. Author(s) of the complete paper

Kraepelin E. manic-Depressive Insanity and Paranoia. Edinburgh: Thoemmes Press, 2002

b. Editor(s) as authors.

Yatham N, Kusumakar V, Kutcher S, editors. Bipolar Disorder. A Clinician's Guide to Biological Treatments. New York: Brunner-Routledge, 2002

Gasto C. Historia. In: Vieta E, Gasto C, editores. Trastornos bipolares. Barcelona: Springer-Verlag Ibérica, 1997

c. Book Chapter
Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press, 1995

III. Other Sources
a. Audiovisual material
HIV+/AIDS: the facts and the future [videocassette]. St. Louis (MO): Mosby-Year Book; 1995

b. Electronic material
Online Journal
Tsui PT, Kwok ML, Yuen H, Lai ST. Severe acute respiratory syndrome: clinical outcome and prognostic correlates. Emerg Infect Dis [serial online] 2003 Sept [date cited]. Available at: http://www.cdc.gov/ncidod/EID/vol9no9/03-0362.htm

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