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Emotions, anxiety, depression and the immune system: an integrative view of psychoneuroimmunology from a meta-analytic review of the narrative

Emociones, ansiedad, depresión y sistema inmunológico: una visión integradora de la psiconeuroinmunología desde una revisión meta-analítica de la narrativa

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SUMMARY

The study focused on conducting a meta-analytic review of three variables psychoneuroimmunology, emotions, and the immune system, intending to find a relationship between them. The methodology was the PRISMA statement with inclusion criteria: production of the last five years, full text, exclusion criteria: book chapters, reviews, editorials, letters to the editorials, as well as systematic and meta-analytic reviews; a formula was created from the variables with Boolean operators (AND, OR, NOT) in databases: Web of Science, PubMed and Elsevier. The first sweep denotes (n=2237) articles and after the application of the screening, the final sample was (n=26). Among the findings is the emergence of three categories of analysis using a word map: cognitive abilities, mental fatigue, and stressors. In conclusion, psychoneuroimmunology is a science that articulates mental processes and the functioning of the nervous, immune, and endocrine systems that affect the individual in such a way that the psychological aspects linked to emotional management and control can present better management and intervention in mental illnesses.

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Keywords: *Anxiety, depression, emotions, immune system, psychoneuroimmunology.*

RESUMEN

El estudio se centró en la realización de una revisión meta-analítica de tres variables psiconeuroinmunología, emociones, y el sistema inmunológico, con la intención de encontrar una relación entre ellos. La metodología fue la declaración PRISMA con criterios de inclusión: producción investigative de los últimos cinco años con texto completo; y criterios de exclusión: capítulos de libros, reseñas, editoriales, cartas a los editoriales, así como revisiones sistemáticas y meta-revisiones analíticas; se creó una fórmula a partir de las variables con operadores booleanos (AND, OR, NOT) en bases de datos: Web of Science, PubMed y Elsevier. El primer barrido arrojo (n=2237) artículos y después de la aplicación del cribado, la muestra final fue (n=26). Entre los hallazgos se encuentra la aparición de tres categorías de análisis utilizando un mapa de palabras: capacidades cognitivas, fatiga mental y factores estresantes. En conclusión, la psiconeuroinmunología es una ciencia que articula los procesos mentales y el funcionamiento de los sistemas inmunológicos y endocrinos son afectados por los aspectos psicológicos relacionados con el manejo y control emocional, siendo necesario un mejor manejo e intervención de estos en las enfermedades mentales.

Palabras clave*: Ansiedad, depresión, emociones, sistema inmunológico, psiconeuroinmunología-*

INTRODUCTION

Positive and negative emotions have generated in individuals diverse experimentations that have allowed linking the mind-body duality by analyzing the attitudes and mental habits that are associated with studies linked to psychoneuroimmunology (1), which has been described as the science that investigates the association between the psyche and the immune systems; identifying that there is a strong influence of the emotional management and control that individuals have on the functioning of the pituitary gland; thus implying that when experiencing an emotion this performs a transformation process that is related to a physical activity, which has an impact on the body, a situation that is explained through the reception of emotional inputs that trigger organic reactions. Psychoneuroimmunology is one of the areas of clinical intervention that approaches health problems and their link with the emotional states that affect the health of human beings (2).

To achieve an intervention from psycho-neuroimmunology and health states in individuals, it is necessary to analyze the interconnections between organic components (biological), psychological (emotional), and environmental (contexts) (3) that are linked to the basis of the elements associated with the states of stress, anxiety, and depression. Because psychotherapists holistically focus their intervention on the dysfunctions that concatenate to trigger organic symptoms that manifest in behavioral patterns (4). In this way, the neuroendocrine system presents neurochemical failures characterized by altered responses in depressive and anxiogenic manifestations, which alter the functioning of neurotransmitters generating clinical indicators, affecting the adrenal autonomic system and with it its incidence in mood affectations; creating collateral effects that influence glutamatergic neurotransmission that requires pharmacological and psychological interventions to inhibit the effects linked to the central nervous system (5).

The relationship between the immune, endocrine, and central nervous system is articulated from the functioning and regulation between hormones and neurotransmitters, generating an autonomous defence system in the organism that has an association of reciprocal modulation between immunocytes, the reticuloendothelial and hematopoietic systems that influence the regulation of hormone production levels and on the psychological variables that present experimental evidence associated to the behavioral patterns that explain the health-disease dyad in individuals (6), identifying the dysfunctions associated to the pathologies that are presented from the emotional substrate, which influences from the theological postulate and the receptor functions coming from the stimuli that affect the corporal systems from the position of the biological base, explainable from the methods of neuropathology in relation to the holistic position of the mind and the body (7).

For its part, mental health from the positive dimension has been defined as a complete state of well-being that includes physical, mental, and social aspects (8). Understanding in this way that when speaking from the integrity of the sphere of health, it is necessary to mention the emotional component, because the brain within its functions generates substances that stimulate neurotransmitters that are connected to the immune system, thus generating defences in the body and activating changes from the immune system (9). So from the neuroimmune factors it has been established that the connection between emotional factors and perceived vulnerability significantly increases the risks of suffering from major diseases because it generates more symptoms and increases the presence of negative emotions due to dissatisfaction that is linked to the factors of psychological discomfort and inhibitory personality patterns (10).

Therefore, the relationship between mind and body is adjusted to the emotional processes and how thoughts originated, linking these components to the levels of satisfaction with life, an increase of psychological well-being, and thus an increase of health determinants that are fundamental in human beings (11); because the responses that are generated from the immune system, represent physical and emotional psychic aspects that are adjusted to the aspects that determine the social and cultural components that allow the increase of the states of satisfaction with oneself and that lead to increase directly the states of health, due to the subjective expressions and self-representation that affect the manifestation of symptoms that are assumed by the individual from an experimental perspective (12).

The biopsychosocial processes of the individual are linked to cognitive factors and the existing relationships between the central nervous system, endocrinology, and immunology (13), because the information that comes from the environmental determinants fulfil a regulation function between the events and how they are perceived, determining in this way that the greater the increase of positive emotions such as joy, optimism, love, the greater the increase of health determinants presented by the subject; thus suggesting that the specific aspects related to emotional regulation and biological immunity are presented satisfactorily if there is a positive correlation with psychic states, providing explanatory support for the relationship between pathogenic factors and the link with attitudes, thoughts and personality traits (14).

Finally, psychoneuroimmunology is fundamental to achieving an understanding of the psychological factors related to diseases of the body, the proper management of emotions will allow you to improve and contribute to patient treatments, establishing the articulations that exist between behavior and the constitution of some diseases in the body (15). Determining the significant increases in states of well-being that are associated with increases in health determinants that lead individuals to develop relational aspects with self-care processes in favor of mental health status and the increase of positive emotions as a defence strategy from the functioning of the autoimmune system (16).

METHOD (PRISMA)

The prism statement performs documentation employing a systematic review of the literature, employing which first identification of the scientific advances in the subject is made, to be subsequently selected according to the inclusion criteria to evaluate and synthesize the corresponding studies that provide a state of knowledge from the approach of a research question that seeks to study a particular phenomenon (17).

Thus, the analysis of observational documentation evaluates the evidence from a quantitative synthesis of the results obtained from an iterative process that analyzes the retrospective contributions, synthesizing the findings in an organized manner, where the biases of systematic reviews are reduced (18).

Inclusion criteria

Among the aspects taken into account for the processing of the information, intellectual production published in the last five years was identified, in studies under full text, which had

as a characteristic a variable associated with the subject of analysis, in the English language, with adult participants (19).

Exclusion criteria

We excluded texts related to book chapters, reviews, editorials, letters to publishers, as well as systematic and meta-analytic reviews, documents in languages other than English, and findings outside the range of the last five years and whose samples were not representative (20).

Search strategies

The search was conducted in specialized databases, which were selected according to the thematic relevance in the areas of health, in line with the reports of advances that incorporate interventional treatments in the area of psychoneuroimmunology and its relationship with emotions in individuals from the psychopathological perspective of diseases such as depression and anxiety as shown in Table 1.

Emotion AND psychoneuroimmunology OR anxiety NOT symptoms; Emotion AND psychoneuroimmunology OR depression NOT dysfunctions; Positive health AND system OR immune NOT stress; Immune system AND neuroendocrine OR cortisol NOT suppression; Health AND disease OR neurogenesis NOT abilities; Emotional AND pathogens OR glucocorticoids NOT effects; Immune system AND emotional OR hypothalamus NOT mechanisms; Emotional AND treatments OR depression AND anxiety OR affective states NOT manifestations.

Data collection process

The analysis of the documents was based on the PRISMA system that takes into account the inclusion of information through evidence, reviewing the relevant findings on the subject that included the analysis of the variables taking into account the contributions made by the scientific community, taking into account that advances in mental health are focused from the perspective of psychoneuroimmunology because the trend in intervention indicates that patients with pathologies or dysfunctions have a high probability of rehabilitation. After all, the different states of mind present direct repercussions on the health status of individuals (Table 1).

Search equations

Table 1. Information search criteria

Databases	Equations in data bases
Web of Science	Emotion AND psychoneuroimmunology OR anxiety NOT symptoms; Emotional AND treatments OR depression AND anxiety OR affective states NOT manifestations. Emotion AND psychoneuroimmunology OR depression NOT dysfunctions.
PubMed	Immune system AND emotional OR hypothalamus NOT mechanisms; Positive health AND system OR immune NOT stress; Emotional AND pathogens OR glucocorticoids NOT effects.
Elsevier	Immune system AND neuroendocrine OR cortisol NOT suppression; Emotional AND treatments OR depression AND anxiety OR affective states NOT manifestations. Emotion AND psychoneuroimmunology OR anxiety NOT symptoms

Own elaboration (2023)

Table 2. Cross-referencing of search terms in the databases.

Crosses/ databases	Web of Science	PubMed	Elsevier	Total
Emotion AND psychoneuroimmunology OR anxiety NOT symptom, Immune system AND emotional OR hypothalamus NOT mechanisms	321	125	157	603
Emotional AND treatments OR depression AND anxiety OR affective states NOT manifestation; Positive health AND system OR immune NOT stress	432	256	243	931
Emotion AND psychoneuroimmunology OR depression NOT dysfunctions; Emotional AND pathogens OR glucocorticoids NOT effects	467	147	89	703
Total	1 220	528	489	2 237

Own elaboration (2023)

Table 3. Process of identification, elimination, and selection of articles.

Equation	Databases	No filtering	No access	Revisions/ Incomplete/ Duplicates	Not met Criteria	Selection
Emotion AND psychoneuroimmunology OR anxiety NOT symptom, Immune system AND emotional OR hypothalamus NOT mechanisms	Web of Science PubMed Elsevier	1 220	545	512	154	9
Emotional AND treatments OR depression AND anxiety OR affective states NOT manifestation; Positive health AND system OR immune NOT stress	Web of Science PubMed Elsevier	528	348	180	169	11
Emotion AND psychoneuroimmunology OR depression NOT dysfunctions; Emotional AND pathogens OR glucocorticoids NOT effects	Web of Science PubMed Elsevier	489	284	205	199	6
Total		2 237	1 177	897	522	26

Own elaboration (2023)

Selection of the studies

The selected studies were based on the analysis of the variables that imply dual pathologies in the processes of mental health affectation in the area of psychoneuroimmunology. The main articles were reviewed from the databases, applying Boolean equations, and then the information was classified by eliminating duplicate files (18) (Table 2).

The selection of the articles was carried out taking into account the observation window of the last five years, taking into account the compliance of the variables studied, subsequently, the studies that were duplicated or did not meet the criteria were eliminated, additionally, the publications that were available in the full text were taken into account, eliminating the abstracts and research notes (19) (Table 3).

Data extraction

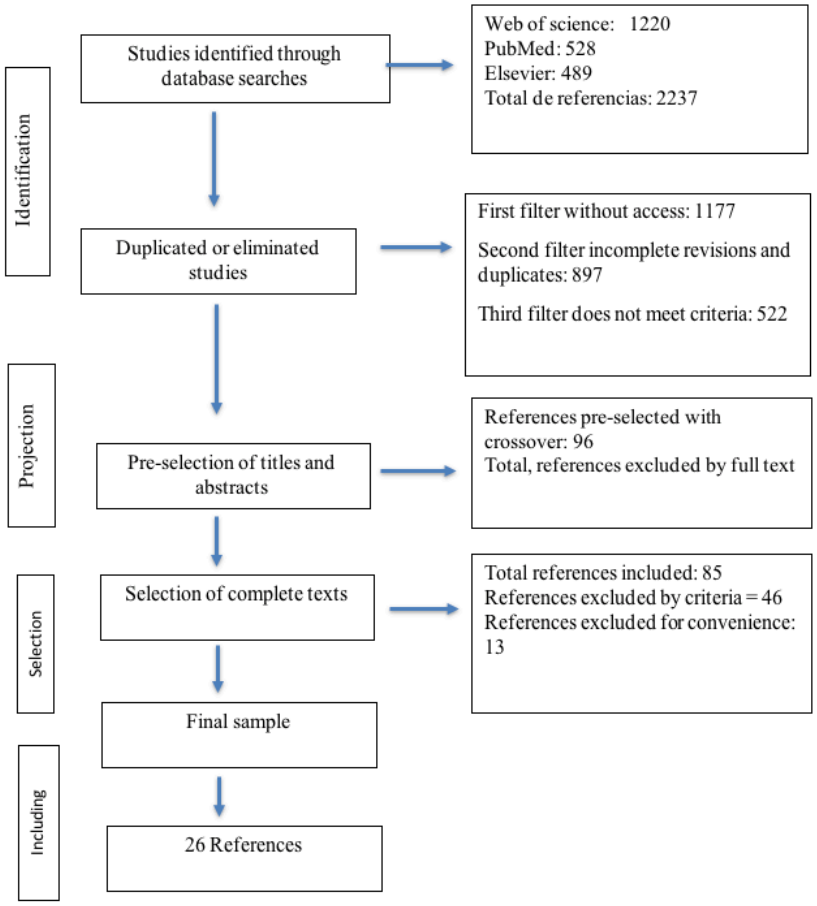

Figure 1. Flowchart of the process of study selection.

Word map

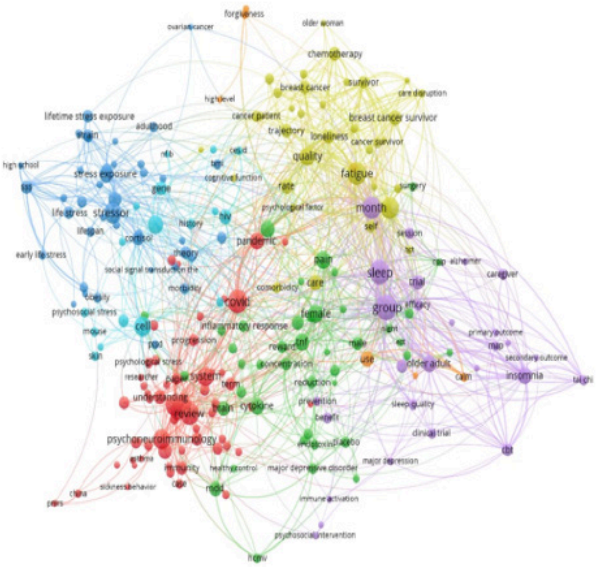

Figure 2. VOSviewer Word Networ.

According to what is expressed in the figure and in relation to the study variables, three categories of analysis are denoted as follows:

Cognitive functions or skills

They are defined as the mental processes that allow the individual to receive, process, and elaborate information, taking an active role in the sensory perception of the surrounding environment (21). These allow learning, storage, and comprehension processes to be carried out in the integration of information processing, thus playing an important role in decision-making and dual execution. Determining that the link between emotions and thinking generates positive behaviors that allow the control of mental states related to the psychological response that is linked to information processing and the formation of thought (22).

This indicates that behavioral determinants are linked to the experience of situations and experiences that are related to feelings (23). Thus, the link between behavior and the brain is presented in an interdependent manner but correlated through the development of socio-emotional skills that integrate the regularization and evaluation of thought from the articulation with positive or negative emotions that lead to the experience of well-being, the strengthening of social skills and healthy relationships that influence health components (24).

Mental fatigue

Fatigue is a state that presents a lack of energy and motivation, as well as symptoms related to drowsiness, apathy, boredom, and emotional stressors, this emotional fatigue leads to the experience linked to the appearance of headaches, muscle tension, and breathing difficulties, among others (25). Within this there is an alteration that affects the decrease in mental functioning, which leads to emotional states presented negatively hindering concentration, skill development, and attentional processes that directly affect feelings

and emotions, increasing the risks of the onset of heart disease and chronic diseases that have a negative impact on mental health (26).

One of the problems that have a greater impact on mental health is the appearance of depressive and anxious conditions that trigger other comorbid pathologies, among which fibromyalgia and cancer stand out, due to the threats and the experience of organic reactions that have a direct impact on internal and external factors that cause psychological disorders and alterations in the central nervous system, due to immunological reactions caused by stress (27); the presence of acute and chronic diseases and immunoregulation disorders and the appearance of neuropsychiatric markers that interfere in the ability to develop activities of daily living that present physical, mental and emotional chronicity due to the difficulty they present in finding a balance in the linking of states of well-being (28).

Stressors

Stress is an emotional response generated by the perception of threats and the security of individuals that are identified in the alteration of neuronal and endocrine functions that impede the psychological adjustment in the human being (29). In this way, the interactions that occur between the nervous system and the immune system present alterations in the adrenergic neurotransmitters obstructing the neuropeptides that prevent a regulation between the central nervous system and the immune system that is linked to the immunosuppression behavior product of the psychophysiological changes that occur in the brain in the face of threatening responses (30).

For the above-mentioned (31), the pituitary ovens present pathophysiological alterations through the chromaffin cells and the activation of the adrenal medulla that generate in the individual an autoimmune response linked to the growth, maturation, and functioning of the immune system (32). Thus, the activating and inhibitory effects of adrenocorticotropic hormones release corticotropin that acts on activated lymphocytes and glucocorticoid receptors that prepare the individual to generate neuromodulation in the synaptic interconnection that transforms the information from the amygdala to the brain through a bidirectional communication that generates a response to psychological stress and stressful experiences that alter the immune parameters in individuals (33).

RESULTS

The results are presented in Table 4.

DISCUSSION

Psychoneuroimmunology focuses its interventions on the psychic and physical interaction processes that occur in the central nervous, endocrine and immune systems (34), thus generating an integrative vision of the processes of health and disease that occur in the individual from the appearance, course and development of somatic diseases that are linked to the psychological alterations that occur more frequently such as anxiety, depression and stress that involve negative manifestations associated with the extrapolation of the psychological alterations that occur more frequently such as anxiety, depression and stress, course and development of somatic diseases that are linked to the psychological alterations that occur more frequently such as anxiety, depression and stress that involve negative manifestations associated with the extrapolation of feelings and emotions that integrate an approach to health problems that are interrelated in the proper functioning of emotions and their impact on the body (35). Consequently, the relevant manager will help to improve the different interventions that the patient has had in their treatments, and their direct incidence in the forms of behavior that lead to the appearance of symptomatology associated with organic diseases (36).

For its part (37), depression has a direct impact on the immune system causing a decrease in serotonin and noradrenaline levels that cause immune reactions linked to dysfunctions and disorders that produce negative emotions related to frustration, anger, fear, and sadness (38). This affects the organism in the appearance of dual pathologies such as stress, fibromyalgia, and cancer since the deterioration of the patient leads to psychological alterations that make

Table 4.

	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
1	https://doi.org/10.1177709727531221109117	Psychoneuroimmunology of Meditation	2022		Therapeutic Role of Yoga and Meditation Preksha (MP)	New Delhi/ India	25 years	N/A	Meditation may have positive benefits in regulating cognitive and emotional behavior
2	doi:10.1080/10253890.2021.1876658	Oxytocin, cortisol, and cognitive control during acute and naturalistic stress	2021	37 participants	Experimental session of acute stress through videos	California/ USA	22 Years	37 women	Oxytocin may provide women with an anxiolytic and affective effect that favors social synchrony and makes it easier to overcome stressful moments
3	https://doi.1016/j.bbi.2020.04.069	Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and research implications for immunopsychiatry	2020	76 psychiatric patients 109 healthy people	Impact of Event Scale-Revised (IES-R)	Chongqing /China	18 years		Study confirms the severity of the negative psychological impact on psychiatric patients during the COVID-19 epidemic
4	https://doi.org/10.1016/j.h.2021.09.004genosppsych.2021.09.004	A mindfulness meditation mobile app improves depression and anxiety in adults with sleep disturbance: Analysis from a randomized controlled trial	2021	239 participants	Insomnia Severity Index (ISI)	Arizona/ USA	Average age 44.5 years	74.6 % women 40.6 % of the racial population diverse	A meditation app can improve depression and anxiety in adults with sleep disorders.

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	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
5	https://doi.org/10.1038/s41598-020-62652-1	Mindfulness Meditation Activates Altruism	2020	326 participants	Calm app (meditation)	Connecticut/ USA	25 years	58,28% women	The current findings are the first to iden-tify a relationship between mindfulness meditation and cooperation
6	doi:10.1080/13607863.2021.1876636	Early-life stress, depressive symptoms,and inflammation: the role of social factors	2022	3 416 participants	Meditation through mindfulness	Los Angeles/ USA	From 36 years to 97.		The frequency of social contact and social support can moderate depressive symptoms.
7	doi:10.1016/j.bbi.2019.03.004	Depressive Symptoms and Immune Transcriptional Profiles in Late Adolescents	2019	87 participants	Psychosocial questionnaire Depression Scale of the Center for epide-miological Stu-dies	Los Angeles/ USA	18 years		Teens with levels Depressives may be at increased risk of developing immune-related somatic diseases in adulthood.
8	https://doi.org/10.1093/abm/kaab106	Psychological Predictors of Self-reported COVID-19 Outcomes: Results From a Prospective Cohort Study	2022	1 087 participants	Psychological factors survey Patient Health Questionnaire (PHQ-9) Generalized Anxiety Disorder Scale Perceived Stress	United Kingdom	18 years onwards		COVID-19 infection and symptoms can increase among people with distress elevated psychological.

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	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
					Scale The scale of Positive and Negative Experiences				
9	https://doi.org/10.1016/j2021.100496.	Neuroinflammation as a pathophysiological factor in the development and maintenance of functional seizures: A hypothesis	2021	12 participants	Hospital Anxiety and Depression Scale (HADS). Profile of Mood States	Alabama/ USA	23 y 50 Years	12 women	This study revealed that the data provided is not sufficient to corroborate the hypothesis. However, psychiatric and immune functioning has given rise to a new field of study called psychoneuroinmulogy.
10	https://doi.org/10.1016/j.abd.2021.04.011	More than a skin disease: stress, depression, anxiety levels, and serum neurotrophins in lichen simplex chronic,	2021	36 participants	Hospital Anxiety Scale Depression Scale Perceived Stress Scale	Istanbul, Turkey	Average age 37 years	7 men 29 women	Patients with Lichen Simplex Chronicus (LSC) are at risk of increased levels of stress, anxiety, depression, impaired quality of life, and decreased levels of neurotrophins
11	https://doi.org/10.1 1770956 7976221079633	Psychosocial Resilience to Inflammation - Associated Depression: A Prospective Study of Breast-Cancer Survivors	2022	270 participants	Center fo for epidemiologic Studies-Depression (CES-D) blood samples for C-reactive	California/ USA		270 Women	The importance of psychosocial resilience by demonstrating a relationship between psychosocial resources and sensitivity to depressive symptoms associated with inflammation.

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	Doi	Title	Year of publication	Sample	Treatment	Country / City	Mean age	Gender %	(Follow-up time)
					protein (CRP) evaluation Event Impact Scale Attachment subscale of the Social Dispositions Scale Revised Life Orientation Test (LOT-R) Pearlin-Schooler Mastery Scale Rosenberg self-esteem scale Positive and Negative Affect Schedule Subscale Mindfulness Awareness Scale				
12	https://doi.org/10.1016/j.physbeh.2021.113324	Age, BMI, and inflammation: Associations with emotion recognition	2021	90 participants	test screen	Birmingham / England	21 to 35 years 63 and 80 years	60% women	Young people with a high BMI performed worse on the RMET compared with their normal BMI counterparts, while the opposite pattern was observed in older individuals.

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	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
13	https://doi.org/10.1186/s13063-020-04242-0	Goal-Focused Emotion-Regulation Therapy (GET) for young adult survivors of testicular cancer: a pilot rando-mized controlled trial of a biobehavioral intervention protocol	2020	60 participants	Goal-Focused Emotion Regulation Therapy (GET)	California/ US	18 and 39 years	Men	GET may have the potential to improve overall adjustment to cancer
14	http://doi.org/10.2147/CIA.S285000	Association Between Systemic Immune-Inflammation Index and Diabetic Depression	2021	2 556 participants	Depression was assessed using the PHQ-9.26 Blood samples	Yanji, China	Average age 61.4 years	1 252 women 1 314 men	Systemic inflammation is a risk factor for depression in patients with diabetes mellitus.
15	https://doi.org/10.3389/fimmu.2020.585294	CD157 and Brain Immune System in (Patho)physiological Conditions: Focus on Brain Plasticity	2020	Mice	CD157 on neuronal and glial cells	Krasnoyarsk, Russia K			CD157 could play a role in the regulation of anxiety and social avoidance
16	https://doi.org/10.2147/JIR.S387588	Evaluation of Inflammatory Response System (IRS) and Compensatory Immune Response	2022	100 participants	Children's Depression Inventory (CDI) Blood test	Zilina, Slovakia	Average age 15.4 years	40 men 60 women	Importantly, the association between the inflammatory response system (IRS) and the compensatory immune response system (CIRS) in adolescent depression appears to be gender-specific.

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	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
		(CIRS) in Adolescent Major Depression							-specific.
17	https://doi.org/10.1038/s41577-021-00508-z	Neuromodulation by the immune system: a focus on cytokines	2021	mice	Cytokine immune molecules	Virginia/ USA			Cytokines can be used to send signals to neurons and thus regulate neuronal activity
18	https://doi.org/10.1186/s13041-022-00902-1	Tumor suppression and improvement in immune systems by specific activation of dopamine D1receptor-expressing neurons in the nucleus accumbens	2022	mice	Sstimulation a repeat of neurons with D1 receptors	Tokyo, Japan			Stimulation of neurons with D1 receptors in the region of the nucleus accumbens suppressed the tumor progression and improved the immune system. It may be a valuable and useful approach to cancer therapy.
19	https://doi.org/10.3390/s22103834	"Listen to Your Immune System When It's Calling for You": Monitoring Autoimmune Diseases Using the iShU App	2022	15 participants	iShU App	Aveiro, Portugal	From the age of 23 to the age of 59.	9 women 6 men	The prototype allows the monitoring of autoimmune diseases before, during and after inflammatory crises, thus responding to personal needs.
20	https://doi.org/10.1371/journal.pone.0272922	Promoting positive emotions and instilling concern for the needs of others during theCOVID-19	2021	237 participants	Hero Program	Buenos Aires, Argentina	12 to 15 years		The Hero program was a useful online application to enhance positive emotions and promote prosocial behavior in uncertain times.

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	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
21	10.2478/rae-2021-0001	Emotions in music and their impact on the emotions of percipients: research on human voice and singing	2021	56 participants	POMS Questionnaire BRUMS Mood Questionnaire	Presov, Slovakia	From 18 years to 44.	34 women 22 men	The sound, the voice, and the singing are relaxing, stabilize the physical and mental state and emotional condition, allowingtoreachacondition of deep concentration.
22	10.3389/ fnbeh.2022.869526	Hypothalamic Neurochemical Changes in Long-Term Recovered Bilateral Subdiaphragmatic Vagotomized Rats	2022 2022	Wistar rats	Vagotomy surgical process	Poland			The results show that, in the long term, vagotomy affects the concentration of hypothalamic amino acids, but not the mRNA expression of the genes analyzed.
23	10.3389/ fnbeh.2022.945661	Acute sleep deprivation disrupts emotions, cognition, inflammation, and cortisol in young healthy adults	2019	23 participants	Pittsburgh Sleep Quality, Depression Scale of the Center for epi-demiological Studies (CES–D)		Average age 20.78	9 women 14 men	Lack of sleep increases negative emotional states such as anxiety, fatigue, confusion, and depression.
24	doi:10.1111/ bjet.12896 10.1097/PSY 0000000000000755	Does emotion matter? An investigation into the relationship between emotions and science learning outcomes in a game-based learning environment	2020	119 participants	Humunology, an educational game Cognitive	Taiwan, China Houston	12 and 13 years		Learning through play Humunology was effective and the long-term effect on learning retention was promising compared to education traditional.

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	Doi	Title	Year of publication	Sample	Treatment	Country/ City	Mean age	Gender %	(Follow-up time)
25	10.1097/ PSY.0000000 000000755	Emotion Regulation and Immune Functioning During Grief: Testing the Role of Expressive Suppression and Cognitive Reappraisal in Inflammation Among Recently Bereaved Spouses	2020	99 participants	cognitive reappraisal	Huston USA		28% men	The use of emotion regulation strategies is associated with a peripheral inflammatory response as measured by peripheral inflammation levels and cytokine levels.
26	10.3389/ fpsyg.2020.566237	Behavioral Immune System Responses to Coronavirus: A Reinforcement Sensitivity Theory Explanation of Conformity, Warmth Toward Others and Attitudes Toward Lockdown		605 participants	RST Personality Questionnaire Anxiety Disorder Questionnaire Generalizada Perceived Vulnerability Scale Patient Health Questionnaire	Plymouth, United Kingdom		426 mujeres 173 hombres	Coronavirus-related behavior is not driven solely by fear, but also by protective and social goals to limit the spread of the virus.

them more prone to develop bidirectional psychophysiological changes between the nervous system and its articulation with the brain, due to the negative psychological manifestations that affect the determinants of health and prevent the harmonious functioning between the psyche and neurotransmitters (39).

With regard to anxiety and the modulation of the central nervous and immune systems, it affects the production of cytokines that affect cortical activation, which modifies the balance of neurotransmitters and their influence on mental pathologies (40). So the relationship with mood directly influences the hypertrophy of the adrenal glands that link emotion with anxiety and depression through the coactivation of the hypothalamic-pituitary-adrenal system characterized by adaptive mechanisms in the release of cortisol and noradrenaline that provides a release pathway induced by negative emotions that generate qualitative and quantitative changes in the anxiogenic behavior of individuals, due to the reception of cognates that generate an imbalance in the cells of the immune system causing hormonal changes that increase the level of cortisol and weaken the immune system due to the manifestations of anxiety (41).

Stress, therefore, distorts the homeostasis of the immune system, increasing the levels of probability of deteriorating health conditions due to the negative changes that occur on the immune system that progressively deteriorates the organism because stressful situations directly affect the functioning of the pituitary gland due to the sympathetic innervation that occurs between the adrenal capsules and the lymph node (42), which brings effects on the central nervous system that according to pathologies such as neoplasia, cancer, anemia, among others, cause adverse effects of psychological and psychiatric nature that are evidenced in cognitive defects, psychotic symptomatology, anorexia, somnolence and suicidal tendencies; explained from the affections and alterations that are presented in the immune system in association with the appearance of psychological stress, where alterations are identified by the immunological changes that influence the appearance of cell migration and inflammatory mediators that lead to neoplastic diseases (43).

Regarding the components of mental health, these can be altered and thus alter the function of the immune system of the subject (44), particularly in the occurrence of stress, which can directly affect emotions, generating dysfunctions in the central nervous system from the secretion of high levels of hormones and chemicals. This is explained by the conditions of association in patients who carry cancer cells, where the presence of alterations in the functioning of the immune system and the acceleration of inflammatory conditions in the body is identified. Originating changes in mood that frequently present depressive and anxiogenic symptomatology that cause alterations in behaviors, through the neurophysiological immunosuppression of the biochemical determinants that modify the central nervous system (45).

CONCLUSIONS

The affectations of the emotional states, generate changes and a series of somatic symptomatologies that are evidenced due to the presence of clinical indicators related to physical pain, eating disorders, and sleep disorders among others, which leads the subject to decrease the immune system and cause alterations in the body, which negatively affect the regulation and control of emotions that are linked to the states of integral health within the proper functioning in the environmental determinant contexts in which it evolves (46). Impacting in this way, the conditions of quality of life that are linked to the health processes in individuals, under the formation of the relational elements between the immune system and brain functioning from the constructs of cortical arousal (47).

The neuroendocrine and immune systems generate developmental processes that are linked to psychological aspects that directly affect human behavior in such a way that the interaction between emotional and mental alterations generates maladaptive situations that lead to the appearance of stress, anxiety, and anxiety, due to the development of pathogens that alternate the functioning of hormones and molecules that are secreted against receptors and immune cells that secrete adrenaline, glucocorticoids, and

noradrenaline among others (48). On the other hand, corticoids are produced under the constancy of the circadian rhythm, increasing the period of stress and increasing the probability of occurrence of chronic pathologies that are linked to the poor control of emotions in daily functioning (49).

Finally, psychoneuroimmunology is a science that articulates mental processes and the functioning of the nervous, immune, and endocrine systems that affect the individual in such a way that the psychological aspects linked to emotional management and control can present better management and intervention in mental illnesses (50). This requires a multidisciplinary intervention process from the contributions of neurosciences, psychology, psychiatry, and neurobiology, to integrate the context of integral health in the individual from the psychosocial factors and in the mind-body interaction.

REFERENCES

1. Peña-Vargas C, Armaiz-Peña G. Behavioral sciences A Biopsychosocial Approach to Grief, Depression, and the Role of Emotional Regulation. Behav Sci (Basel). 2021;11(8):110.
2. Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Emotions, morbidity, and mortality: New perspectives from psychoneuroimmunology. Ann Rev Psychol. 2002;53:83-107.
3. Zachariae R. Psychoneuroimmunology : A bio-psycho-social approach to health and disease. Scand J Psychol. 2009;50(6):645–51.
4. Lugović-Mihić L, Mihatović D, Šitum M. Psychoneuroimmunology and skin diseases. Rad Hrvat Akad Znan i Umjet Med Znan. 2019;537(46-47):25-36.
5. Kautz MM. Applications of psychoneuroimmunology models of toxic stress in prevention and intervention efforts across early development. Brain, Behav Immun Heal. 2021;16:100322.
6. D'Acquisto F. Affective immunology: Where emotions and the immune response converge. Dialogues Clin Neurosci. 2017;19(1):9-19.
7. Jaremka LM, Lindgren ME, Kiecolt-Glaser JK. Synergistic relationships among stress, depression, and troubled relationships: insights from psychoneuroimmunology. Depress Anxiety. 2013;30(4):288-296.
8. Littrell JL. The Importance of Psychoneuroimmunology for Social Workers. Fam Soc. 2019;100(1):17-33.
9. Shields GS, Spahr CM, Slavich GM. Psychosocial Interventions and Immune System Function: A Systematic Review and Meta-analysis of Randomized Clinical Trials. JAMA Psychiatry. 2020;77(10):1031-1043.
10. Murray DR, Prokosch ML, Airington Z. PsychoBehavioroimmunology: Connecting the behavioral immune system to its physiological foundations. Front Psychol. 2019;10:1-7.
11. Ulloa A, Sánchez R. Metaconocimientos de los estados emocionales de estudiantes de educación superior Meta-knowledge of the emotional states of higher education students. Cienc Lat Rev Científica Multidiscip. 2022;7:445-459.
12. Hernández-Flórez N, Moncada-Navas F, Lhoeste-Charris A, Klimenko O, Ortíz-González A. Habilidades de pensamiento crítico creativo e inteligencia emocional en estudiantes universitarios: Una revisión bibliométrica desde la literatura. Cienc Lat Rev Científica Multidiscip. 2022;6:2029-2054.
13. Molina J. Psiconeuroinmunología: una propuesta no inmune a la critica. Cent Centroaméricano José Simeón. 2020;1(1):15-18.
14. Hernández-Flórez N, Leal-Leal GA, Mogollón-Canal OM, Moreno-Salgado A, Rodríguez-Rivera D, Vergel-Rodríguez C, et al. Variables de personalidad y estilos de vida saludable en estudiantes universitarios de la Corporación Universitaria Minuto de Dios en el centro regional Cúcuta. Inf Psicológicos. 2020;20(2):83-94.
15. Pérez L, Moré C, González Y, Alemán A. Psychoneuroendocrinoimmunology: Claim for a comprehensive vision in medical studies. Edumecentro. 2019;11(3):254-261.
16. Jara C, Acuña L, Gengler J. Estrés e Inmunidad. Medwave. 2001;1(11):171-174.
17. Sánchez-Serrano S, Pedraza-Navarro I, Donoso-González M. How to conduct a systematic review under PRISMA protocol? Uses and fundamental strategies for its application in the educational field through a practical case study. Bordon Rev Pedagog. 2022;74(3):51-66.
18. Hutton B, Catalá-lópez F, Moher D. La extensión de la declaración PRISMA para revisiones sistemáticas que incorporan metaanálisis en red: PRISMA-NMA. Med Clin (Barc). 2016;(xx):10-14.
19. Page M, McKenzie J, Bossuyt P. Declaración PRISMA 2020: Una guía actualizada para la publicación de las revisiones sistemáticas. Rev Esp Cardiol. 2021;74(9):790-799.
20. Barrios-Serna K, Orozco-Núñez D, Pérez-Navas E, Conde-Cardona G. Nuevas recomendaciones de la

versión PRISMA 2020 para revisiones sistemáticas y metaanálisis. Acta Neurol Colomb. 2021;37(2):105-106.

21. Benavidez V, Flores R. La importancia de las emociones para la neurodidáctica The importance of emotions for the neurodidactics Introducción Los resultados de las investigaciones actuales en el campo de las Neurociencias. Wimblu Rev Estud Psicol. 2019;14(1):25-53.
22. Bueno D. La neurociencia como fundamento de la educación emocional Neuroscience as a Basis of Emotional Education Introducción. Rev Int Educ Emoc. 2021;1:47-61.
23. Bitzer-Quintero OK, Ortiz GG, Jaramillo-Bueno S, Ramos-González EJ, Márquez-Rosales MG, Delgado-Lara DLC, et al. Psycho-Neuro-Endocrine-Immunology: A Role for Melatonin in This New Paradigm. Molecules. 2022;27(15):4888.
24. Vernaza-Pinz P, Posadas-P L. Dolor y emoción, una reflexión para el profesional en ciencias de la salud. Duazary. 2019;16(1):145-155.
25. Soria V, Uribe J, Salvat-Pujol N, Palao D. Psiconeuroinmunología de los trastornos mentales. Rev Psiquiatr y Salud Ment. 2017;11:115-124.
26. Moscoso MS. Chronic stress and the Mindfulness-Based Cognitive Therapy: A new dimension in psychoneuroimmunology. Pers Rev la Fac Psicol. 2010;(13):11-29.
27. Álvaro T, Traver F. Una visión psiconeuroinmunológica de la fibromialgia. Rev Psicopatol Psicol Clín 2010;15(3):149-163.
28. Linares V, Rivero R, Piqueras A, García L, Armando L. Psiconeuroinmunología: conexiones entre sistema nervioso y sistema inmune. Suma Psicológica. 2008;15(15):115-142.
29. Andrea D, Actis M, Dra P, Outomuro D. Medicine and stress: Historical background and scientific evidence. Gac Méd Caracas. 2018;119(3):183-187.
30. Solano R, Velásquez V. Efecto inmunomodulador del estrés psicológico. Bárbula. 2012;16(1):51-57.
31. Kuthati Y, Davuluri VNG, Yang CP, Chang HC, Chang CP, Wong CS. Melatonin MT2 receptor agonist IIK-7 produces antinociception by modulation of ROS and suppression of spinal microglial activation in neuropathic pain rats. J Pain Res. 2019;12:2473-2485.
32. Molina T. Psiconeuroinmunoendocrinología, emociones y enfermedad. MedULA, Rev Fac Med Univ Los Andes. 2009;18:155-163.
33. Sánchez-Teruel D, Robles-Bello M. Psiconeuroinmunología: hacia la transdisciplinariedad en la salud. Educ Médica. 2018;19:171-178.
34. Alessi MG, Bennett JM. Mental health is the health of the whole body: How psychoneuroimmunology & health psychology can inform & improve treatment. J Eval Clin Pract. 2020;26(5):1539-1547.
35. Slavich GM. Psychoneuroimmunology of Stress and Mental Health. The Oxford Handbook of Stress and Mental Health. 2020:518-546.
36. Moraes LJ, Miranda MB, Loures LF, Mainieri AG, Mármora CHC. A systematic review of psychoneuroimmunology-based interventions. Psychol Heal Med. 2018;23(6):635-652.
37. Cohen S, Herbert TB. Health Psychology: Psychological Factors and Physical Disease from the Perspective of Human Psychoneuroimmunology. Ann Rev Psychol. 1996;47:113-142.
38. Ehrlich KB. Attachment and psychoneuroimmunology. Curr Opin Psychol. 2019;25:96-100.
39. Carrico AW, Cherenack EM, Rubin LH, McIntosh R, Ghanooni D, Chavez J V, et al. Through the Looking-Glass: Psychoneuroimmunology and the Microbiome-Gut-Brain Axis in the Modern Antiretroviral Therapy Era. Psychosom Med. 2022;84(8):984-994.
40. Zachariae R. Psychoneuroimmunology: A bio-psycho-social approach to health and disease. Scand J Psychol. 2009;50(6):645-651.
41. Sturmberg JP. Health and Disease Are Dynamic Complex-Adaptive States Implications for Practice and Research. Front Psychiatry. 2021;12.
42. González-Díaz SN, Arias-Cruz A, Elizondo-Villarreal B, Monge-Ortega OP. Psychoneuro-immunoendocrinology: Clinical implications. World Allergy Organ J. 2017;10(1):19.
43. Chen MA, Leroy AS, Majd M, Chen JY, Brown RL, Christian LM, et al. Immune and Epigenetic Pathways Linking Childhood Adversity and Health Across the Lifespan. Front Psychol. 2021;12:788351.
44. Benros ME, Waltoft BL, Nordentoft M, Ostergaard SD, Eaton WW, Krogh J, et al. Autoimmune Diseases and Severe Infections as Risk Factors for Mood Disorders A Nationwide Study. JAMA Psychiatry. 2013;70(8):812-820.
45. Kelley KW, Peng Y, Liu Q, Chang H, Spencer SJ, Hutchinson MR, et al. Psychoneuroimmunology goes East: Development of the PNIRS China affiliate and its expansion into PNIRS Asia-Pacific. Brain Behav Immunity. 2020;88:75-187.
46. Seiler A, von Känel R, Slavich GM. The Psychobiology of Bereavement and Health: A Conceptual Review From the Perspective of Social Signal Transduction Theory of Depression. Front Psychiatry. 2020;11:565239.
47. Shields GS, Kuchenbecker SY, Pressman SD, Sumida KD, Slavich GM. Better cognitive control

of emotional information is associated with reduced pro-inflammatory cytokine reactivity to emotional stress. Stress. 2016;19(1):63-68.

48. Capuron L, Castanon N. Role of Inflammation in the Development of Neuropsychiatric Symptom Domains: Evidence and Mechanisms. Brain Imaging Behav Neurosci. 2012;289-320.

49. Chen Y, Baram TZ. Toward understanding how early-life stress reprograms cognitive and emotional brain networks. Neuropsychopharmacology. 2016;41(1):197-206.

50. Schulz KH, Gold S. Psychische belastung, immunfunktionen und krankheitsentwicklungen. Die psychoneuroimmunologische perspektive. Bundesgesundheitsblatt - Gesundheitsforsch - Gesundheitsschutz. 2006;49(8):759-772.