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Review Article

Clinical Importance of Anxiety, Depression and Psychoneuroimmunoendocrinology

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Abstract

Anxiety (A) and Depression (D), two major clinical entities related to both health and illness, are overlooked now a days in health care settings. The first objective of this review is to show the important correlation between A and D and various diseases. The second objective is to present a modern approach so that A and D are considered by healthcare teams as playing a key role in different work areas, including primary care. The third objective is to emphasize the importance of combining Psychopharmacology and Psychotherapy to treat both A and D in relation to co-occurring illnesses, together with the contributions of Scientific Psychosomatics and Psychoneuroimmunoendocrinology (PNIE).

Keywords: Anxiety; Depression; Psychosomatics; Psychotherapy; Psychopharmacology; Psychoneuroimmunoendocrinology

Abbreviations

S: Stress; A: Anxiety; D: Depression; PNIE: Psychoneuroimmunoendocrinology; COPD: Chronic Obstructive Pulmonary Disease; CV: Cardiovascular; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein

Introduction

Anxiety (A) and depression (D) are two underestimated entities in clinical practice nowadays. These diseases are present in mental health consultations as well as in other specialties, particularly in those related to primary care. "A and D are subjects of interest not only for psychiatrists." [1]. Stress (S), A and D are frequently considered as similar entities; however, they are different, well-categorized disorders. Stress is the first reaction a person is exposed to when coping with vital situations. The term "stress" should be restricted to conditions where an environmental demand exceeds the natural regulatory capacity of an organism, in particular situations that include unpredictability and uncontrollability, that is, from the physiological viewpoint, stress seems characterized by either the absence of an anticipatory response (unpredictable) or a reduced recovery (uncontrollable) of the neuroendocrine reaction. Anxiety, a physiological response necessary for all human beings to survive, appears later, once the first stage, stress, has been overcome. It helps protect individuals in dangerous situations and prepare them for challenges. Anxiety may be either channeled, for example, into a positive action, or eliminated, or may develop as a somatic symptom. If it persists and certain hereditary, environmental, social, and behavioral factors are present, anxiety may trigger depression. The term depression defines a syndrome characterized by emotional dejection, low self-esteem, and a decrease in the capacity to feel pleasure. These symptoms are usually accompanied by affective, behavioral, cognitive, vegetative and motor manifestations which seriously affect quality of life and socio-occupational performance. From the point of view of Psychiatry, the term depression has at least three meanings. It may refer to a symptom, a syndrome, or a nosologic entity. Therefore, S, A and D must be correctly differentiated and diagnosed to enhance the quality of life of the patient, and as a consequence, therapeutic results will be improved once appropriate treatments and their protocols are carried out.

This article aims at reviewing only some of the references in the vast literature published on the association between A, D and various diseases, which supports that these two disorders do not belong exclusively to the field of Psychiatry. Accordingly, this review is made with the contributions of PNIE, a modern integration paradigm or physiopathological construct that shows the immune, endocrine, neural and behavioral systems fundamentally interact in a network and are integrated as only one system capable of reacting to certain events, such as stressful situations. Hence, a therapeutic and diagnostic method, that is, "a simultaneous double approach", is presented to integrate clinical evaluations, diagnostic methods, Psychopharmacology, Psychotherapy, among other assessment instruments medical professionals have nowadays.

This review was conducted using the contributions of Scientific Psychosomatics, PNIE, and the publications consulted in the RIMA (Red Informática de Medicina Avanzada, www//http.rima.org/), sponsored by the PAHO (Pan-American Health Organization).

Literature Showing the Association of A and D with Various Diseases

Disorders related to gynecology and obstetrics

A systematic review was done with patients suffering from polycystic ovary syndrome in whom follow-up studies detected anxiety and depression. It was found that women with this syndrome had a higher mean tendency to A and D than healthy control subjects [2].

A study carried out on the daughters of depressed mothers, the relationship with different stressful events and the prediction of psychiatric disorders, concluded that interpersonal stress and depressed mothers were indeed important factors to develop psychiatric diseases [3]. The prevalence of A and D in the post-partum period is well-known; therefore, in the six months following birth,

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preventive measures were reinforced to reduce anxiety and depression symptoms. The findings showed that coordinated and integrated measures for prenatal care may contribute to the prevention and reduction of A and D during the postpartum period [4]. In a study conducted by Mott SL et al, A and D were compared in puerperal birth mothers and in adoptive mothers in order to find differences between both groups. The levels of depression were not significantly different but adoptive mothers did experience more anxiety. In addition, these adoptive mothers had more depression symptoms during the years following adoption; therefore, it was suggested that A and D should be evaluated in these mothers as well [5]. Blackmore ER et al. concluded that D and A associated to miscarriages showed a persisting pattern after successful pregnancies; consequently, proper interventions to improve A and D conditions will ensure healthy pregnancies [6]. It has also been noted that during the first year following the diagnosis of breast cancer, A and D are often the cause of recurrence of said disease [7]. In a study on female cancer patients, Zenger et al analyzed levels of pessimism, which was considered to be a high risk factor in A and D levels. They arrived at the conclusion that "it seems to be more important not to be pessimistic than to be optimistic" in relation to A and D [8].

Diseases of the cardiovascular system

In patients with cardiovascular disease A and D pre-exist simultaneously, on average, 17 years before the event. The synergic action upon D and A was assessed to enhance health care of patients with cardiovascular disease [9]. Other investigators observed that depression in coronary patients is related to adverse outcomes, including death and non-fatal cardiac events, such as myocardial infarction and angina pectoris. Thus, in line with these findings, depression must be routinely detected and the role played in the recovery process should not be underestimated [10]. In an experimental study, four models of rodents were found fit to work on A and D affective disorders [11]. In the process of searching for biochemical markers linked to A and D, it was demonstrated that increased High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) were associated with impairment of the Cardiovascular condition (CV), among others [12]. D and A were also correlated with increase in the lumen of blood vessels, an early manifestation of arterial hardening; therefore, exposure to D and A may result in the development and progression of atherosclerosis and other cardiovascular conditions [13].

Allergy, Asthma and other diseases of the respiratory system

When correlating gender, depression and hospitalization risk, Fan VS et al. concluded that depression symptoms were common in patients with Chronic Obstructive Pulmonary Disease (COPD) history; however, few of them received treatment [14]. The relationship between the severity of asthma and co-morbidity with A and D disorders was studied. The findings supported data of high A and D morbidity in patients with asthma, irrespective of the severity of the event [15]. The conclusions of another study relating a topic and D provided evidence that D potentially contributes to allergic disorders [16]. The study of levels of D, A, behavioral problems and the frequency of psychiatric disorders in children with chronic idiopathic urticaria, led to conclude that children have high psychiatric morbidity, suggesting also that their psychiatric condition should be assessed when chronic idiopathic urticaria is present [17]. A study conducted by Trzcinka H et al. analyzed the relationship between anxiety and depression and the degrees of severity of asthma. They found that there was a significant severity in asthma patients with anxiety and depression in comparison with the control group [18]. Children with anxiety disorders had high rates of chronic diseases, such as asthma and other allergies [19]. Parents' separation or divorce is an important cause of anxiety in children and adolescents [20]. According to the conclusions of a research evaluating autonomic activity in children with anxiety disorders, the use of a battery of tests plays an important role to differentiate anxious from non-anxious children [21]. Measurement scales for A and D in cases of rhinitis paved the way to find the cause of these conditions (A and D) in patients suffering from allergic rhinitis [22]. In the area of immune- allergy interrelated with PNIE; it was proved that there is a positive association between allergic disorders and anxiety, and a positive trend between allergic diseases and depression [23]. Furthermore, A and D showed dysregulation of tissue growth factor (glycolysis), an identified factor that would open promising doors for the diagnosis and treatment of both entities [24]. Regarding the etiology of D, the role of the oxidative and nitrosative stress pathway was investigated. It was concluded that this is an important metabolic pathway contributing to the diagnosis and treatment of D [25].

Further literature related to anxiety and depression

When A and D were assessed in patients with renal transplants, it was found that A was a major symptom with low impact on receptors while D was more prevalent in transplanted patients [26]. A study on the prevalence of anxiety disorders in medical clinic yielded the following results: neurology (24, 7%), respiratory medicine (20, 9%), gastroenterology (19, 5%), cardiology (19, 1%) and endocrinology (17, 5%) [27]. With regard to phobias, in Finland, a study was undertaken to determine A and D in relation to fear when visiting the dentist. A and D co-morbidity was reported to be statistically significant when fear appeared during consultation [28]. Concerning arthritis, the findings of a study conducted by Murphy LB et al. involving 1,793 patients showed that 18% of the subjects presented D, and 31% A, that is to say, the presence of the latter was twice as common as the former [29]. Gavic, L et al. found a high correlation between A, D, and psychological stress with symptoms of aphthous stomatitis and oral lichen planus [30].The results of a study by Motaal Gomaa MA et al. support that D, A and stress should be taken into account in the treatment of patients suffering from tinnitus [31]. Even though patients admitted to the Observation Care Unit experienced A and D, the symptoms were poorly recognized by the physicians of the Unit [32]. Finally, another relevant finding was that subjects with intestinal inflammatory disease (Crohn's disease, ulcerative colitis) should be also examined for A and D [33].

The Psychoneuroimmunoendocrinology network

Another objective of this review article is to highlight the importance of the psychoneuroimmunoendocrinology paradigm for the diagnosis and treatment of A and D. Well-known authors consider that biological/ conceptual models and technical aspects of psychoneuroimmunology play an important role when dealing with pediatric populations; these authors also give insights into the rationales and benefits of integrating hypotheses in connection with

neuro inflammation in studies of developmental psychopathology [34].

Psychoneuroimmunologic findings in various diseases have proved to be of great relevance [35]. A brief commentary on psychoneuroimmunology, the whole and the sum of its parts, refers to the importance of relaxation as an alternative method, thus showing the beneficial effects of this paradigm which integrates the mind and the body. PNIE, that is Psychoneuroimmunology, focuses on multidisciplinarity and avoids reductionism [36]. In agreement with these findings, Haroon E et al. make reference to the meeting of psychoneuroimmunology and neuropsycopharmacology and the translational implications of the impact of inflammatory mechanism upon behavior, specifically on D, providing elements of the basic sciences that may be applied to the clinical sciences together with PNIE [37].

The present article also reviews the social and behavioral factors acting on the brain that influence health, illness, and death. Using data from several areas of research, a new paradigm is proposed for understanding health and illness. This paradigm, Psychoendoneuroimmunology (PNIE), provides both the concepts and the mechanisms for studying and explaining mind-body relationships. It is a well-accepted fact that the brain is the body's first line of defense against illness, and the mind is the functioning of the brain. PNIE incorporates ideas, belief systems, hopes, and desires as well as biochemistry, physiology, and anatomy. As we change our thoughts, we are changing our brain and thus, our biology and our body. Belief systems set a baseline for the brain upon which other variables will act and have their effects. It should be remembered that there are four continually interacting information processing systems in humans: the mind (psyche); the endocrine system; the nervous system; and the immune system. These four systems continually communicate with each other, and the science and new paradigm of health incorporating all of these systems is PNIE. It´s commented that there is increasing evidence that the Central Nervous System (CNS) can influence the immune response, the body's defense against infectious and malignant diseases. This knowledge on the interactions among the CNS, the immune system, and the endocrine system in regard to mechanisms of action is still limited. With the use of modern technology and the work of brilliant researchers, we are beginning to glimpse how these four systems interact to ensure health, fight disease, and delay death. We are also learning what happens when the systems fail. Fundamental to understanding PNIE is awareness that three of the systems—nervous, endocrine, and immune—have receptors on critical cells that can receive information (via messenger molecules) from each of the other systems. Will be consider the fourth system, the mind (psyche), as the functioning of the brain. Our thoughts, our feelings, our beliefs, and our hopes are nothing more than chemical and electrical activity in the nerve cells of our brain. It is literally true that as experience changes our brain and thoughts, that is, changing our mind, we are changing our biology. This activity of the brain is the body's first line of defense against illness, against death, and for health and well-being. Under optimal conditions, these four systems interact in harmony, which results in homeostasis, an optimal equilibrium that fosters health and combats disease. Many factors influence this interaction—heredity, personality, lifestyle, and environment. When there is an acute disruption of this equilibrium, illness may result. Of particular interest here is psychological stress—stress in the mind—and there are excellent reviews of the nervous, endocrine, and immune system interaction. It must be remembered that there is much mind-body research, which does not in any obvious way involve the immune system. The PNIE paradigm is a heuristic device to encourage new ways of thinking about health and illness [38].

Multi-causality of diseases and scientific psychosomatics

The previous findings have shown the multi-causality of diseases, that is to say, a disease stems from different factors such as, hereditary, genetic, environmental, and infectious factors, among others. In order to offer a physiopathogical explanation, PNIE aspects and tools are associated with these diseases. PNIE enables us to understand and to explain to others the way in which mental, cerebral, behavioral, immunological, and endocrinological systems interact, all fundamentally integrated in a network, harmonized (health) or unbalanced (illness)

Moreover, this review indicates that research in PNIE represents an area of exponential growth within psychosomatic research [39]; thus, PNIE and psychosomatic medicine may be considered a passage to the future. Kiecolt-Glaser, JK et al. suggest that PNIE may have important implications for basic biological sciences as well as for medicine [40].

Finally… to refer to the concept of psychosomatic diseases, linking them to M. Bunges´s words who said that the medical lesson is that scientific psychosomatics is psycho-neuro-endocrine-immunology [41].

Double simultaneous approach: a proposal for modern medical care

In the context of the large body of literature reviewed above and given our experience in the management and treatment of A and D patients, the" double simultaneous approach" is proposed, that is to say, when dealing with a patient with physical or psychological illnesses, or both, treatment should take into account psychological and physical aspects. This proposal is based on the concept that patients are persons, they are body and mind and as such, their problems, whether physical, mental or both should be given thoughtful consideration A physical disorder will surely involve psychological suffering; therefore, patients must be cared for and emotionally supported. Likewise, if a subject comes for consultation about a psychological disorder, we may infer that his soma is suffering or will start to suffer from psychological imbalances. Therefore, when treating an individual with psychological or physical disorders, both aspects should be addressed together. This simultaneous approach, which offers numerous clear benefits for the patients as well as for the therapists, will result in better quality of patient care, better quality of life and enhanced patient satisfaction. Furthermore, we must also bear in mind the large number of resources we have at our disposal: laboratories, images, specific and general medication, psychotherapies and, fundamentally, communication, empathy, understanding, and our training in close connection with Psychosomatics, with PNIE and with this proposed model: "the double simultaneous approach", which is deemed indispensable for health issues in the 21st century, as Ray O states when referring to PNIE and to the change of paradigm this model means [38].

It is worth mentioning that there is literature pointing out the relevance of the differences between psychopharmacology and psychotherapy, but no literature focusing on both therapeutic proposals concurrently applied.

Conclusion

Anxiety and depression are two significant health concerns in current literature. It is essential that all healthcare professionals understand that both disorders must be taken into account when examining patients. The double approach, mental (psychic, emotional) and organic (somatic) is essential for treatments to become more effective, to have fewer therapeutic failures, thereby impacting on patients´ quality of life This double approach directly benefits the patients as well as health professionals, since it contributes to avoid uneasiness and tensions in daily activities. There still remains a long way to go, and further research supported by Psychosomatics and PNIE should be undertaken in the future. Anxiety and depression should be key elements regarding patient care and basic and clinical investigations, and necessarily included in current treatment protocols and therapies.

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