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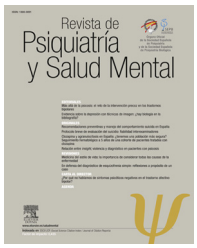

REVIEW ARTICLE

Psychoneuroimmunology of mental disorders☆

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Abstract The immune system is a key element in the organism's defence system and participates in the maintenance of homeostasis. There is growing interest in the aetiopathogenic and prognostic implications of the immune system in mental disorders, as previous studies suggest the existence of a dysregulation of the immune response and a pro-inflammatory state in patients with mental disorders, as well as an increased prevalence of neuropsychiatric symptoms in patients suffering from autoimmune diseases or receiving immune treatments. This study aims to conduct a narrative review of the scientific literature on the role of psychoneuroimmunology in mental disorders, with special focus on diagnostic, prognostic and therapeutic issues. The development of this body of knowledge may bring in the future important advances in the vulnerability, aetiopathogenic mechanisms, diagnosis and treatment of some mental disorders.

PALABRAS CLAVE
Inflamación;
Inmunología;
Autoinmune;
Depresión;
Esquizofrenia

Psiconeuroinmunología de los trastornos mentales

Resumen El sistema inmunitario es una pieza fundamental en la defensa del organismo y participa en el mantenimiento de la homeostasis. Existe un interés creciente en las implicaciones etiopatogénicas y pronósticas del sistema inmunitario en los trastornos mentales, avalado por estudios previos que sugieren la existencia de una disregulación de la respuesta inmune y un estado proinflamatorio en pacientes con una enfermedad mental, así como la elevada

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prevalencia de síntomas neuropsiquiátricos en pacientes con enfermedades autoinmunes o que reciben tratamientos inmunológicos. En el presente trabajo se realiza una revisión narrativa de la literatura científica sobre el papel de la psiconeuroinmunología en los trastornos mentales, especialmente en aspectos diagnósticos, pronósticos y terapéuticos. El desarrollo de este cuerpo de conocimiento puede aportar en el futuro importantes avances en la vulnerabilidad, mecanismos etiopatogénicos, diagnóstico y tratamiento de algunos trastornos psiquiátricos.

Introduction

The first studies of mind–body interaction date from the first half of the 20th century, when the physiologist Walter Cannon coined the term homeostasis in his work ''The wisdom of the body''.[1] He described the physiological mechanisms that intervene in a physical–chemical balance that is essential, and proved that the emotional state of an animal (anxiety, stress or anger) may be accompanied by the stoppage of stomach movements. On the other hand, Hans Selye developed the concept of the general adaptation syndrome, a set of psychophysiological changes which rats suffered when exposed to different harmful agents in the laboratory[2] as a reaction of the organism to new conditions, and which years later he termed ''stress''.[3] In 1975, with the works of the psychologist Robert Ader and the immunologist Nicholas Cohen the term ''psychoneuroimmunology'' was coined, based on studies which showed that an adverse signal channelled through the nervous system led to reactions in the immune system.[4] Due to the fact that immunological factors are often associated with endocrinological factors, sometimes the term ''psychoneuroendocrinoimmunology'' is used. This field of scientific interest would be dedicated to the study of hormonal and immunological aspects of mental disorders. These would include the psychiatric manifestations of hormonal or immunological diseases and those associated with hormonal or immunological treatments.

Notable progress has been made in recent decades in the field of psychoneuroimmunology. Therefore, if PubMed is searched for immunological aspects of mental disorders using the search strategy (immune OR inflammat*) AND (psychiatry OR mental disorder OR schizophrenia OR depression OR bipolar), then a total of 36,127 publications until 2016 are obtained, with an exponential increase in the last two decades (Fig. 1). Progress in this field of knowledge in connection with mental disorders runs from aetiopathological aspects to therapeutic ones. One advance involved the discovery of autoimmune markers that have helped in the diagnosis of some encephalitis symptoms that until recently lacked an exact diagnosis. On the other hand, it has been suggested that anti-inflammatory agents be used in the therapeutic approach for several mental disorders associated with conventional psychopharmacological treatments and psychotherapies.

This paper presents a narrative review of relevant aspects of the immune system in the pathogenesis, clinical expression and treatment opportunities of mental disorders. It also covers aspects in connection with the hormones that are involved in the response to stress, due to their important connection with the inflammatory system and their association with severe mental disorders, as well as some specific stress-related disorders. To undertake this review a search of papers was conducted using PubMed with a time limit commencing in the year 2000. It also occasionally includes earlier classical references and seminal works cited in recent papers or reviews of the same subject.

The immune system

General considerations

The immune system comprises those structures and biological process which defend the organism against aggressions. These may be external (such as pathogenic microorganisms) or internal (such as cancer cells), and the aim is to re-establish homeostasis (for a general review see Delves and Roitt, 2000[5]). The immune system can be classified as ''innate'' (non-specific) and ''acquired'' (specific).

The innate system is the first line of defence of the organism. It includes physical barriers such as the skin and mucus membranes, together with other elements such as phagocytes, including macrophages (which in brain tissue form the microglia) and granulocytes (neutrophils). Acquired immunity is more sophisticated and has delayed action onset. It consists of the recognition and destruction of antigens.

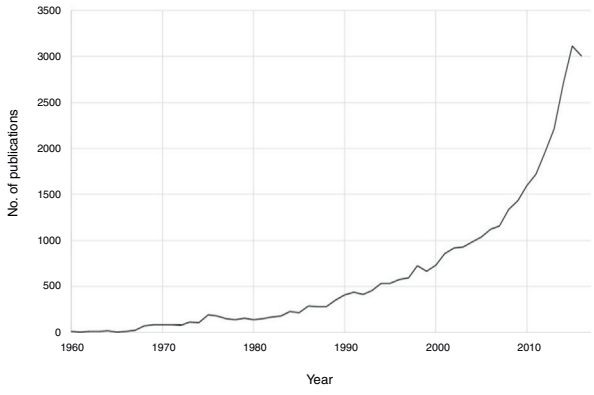

Figure 1 Number of publications per year in psychoneuroimmunology from 1960 to 2016.