



Review article

Pro-inflammatory Cytokines, Biomarkers, Genetics and the Immune System: A Mechanistic Approach of Depression and Psoriasis

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ABSTRACT

Objective: To highlight the inflammatory and immunological mechanisms involved in depression and psoriasis.

Methods: A comprehensive literature search was performed in various databases, in total 145 studies were selected.

Results: Depression and psoriasis have an association. Immune mechanisms —the actions of tumor necrosis factor- α , interleukin 1 (IL-1), IL-2, IL-10, IL-22, IL-17, interferon- γ , IL-1 β , prostaglandin E2, C-reactive protein, IL-6, and IL-8 etc.—, and some genetic changes are involved.

Conclusions: A possible bidirectional relationship of psoriasis and major depression exists; i.e. the depression leads to psoriasis, and psoriasis leads to depression. We recommend more studies in the future to get a deeper and better understanding about this relationship.

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Citocinas proinflamatorias, biomarcadores, genética y sistema inmunológico: un enfoque mecanicista de la depresión y la psoriasis

RESUMEN

Objetivo: Poner de relieve los mecanismos inflamatorios e inmunológicos involucrados en la depresión y la psoriasis.

Métodos: Se realizó en varias bases de datos una búsqueda bibliográfica completa; en total se incluyeron 145 estudios.

Resultados: Hay asociación entre depresión y psoriasis y están involucrados mecanismos inmunitarios —las acciones del factor de necrosis tumoral alfa, las interleucinas (IL) 1, 2, 10, 22 y 17, el interferón gamma, la IL-1 β , la prostaglandina E2, la proteína C reactiva, la IL-6 y la IL-8, etc.— y algunos cambios genéticos.

Palabras clave:

Depresión por psoriasis

Psicodermatología

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Psoriasis y depresión mayor

Depresión por inflamación

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Conclusiones: Hay una posible relación bidireccional entre psoriasis y depresión, es decir, la depresión lleva a psoriasis y la psoriasis lleva a depresión. Se recomiendan más estudios en el futuro para obtener una comprensión más profunda y mejor sobre esta relación.

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Introduction

“Doctor! I have been treated for major depression for the past so many years and now I have developed this silvery skin.” These kinds of statements are occasionally heard in the psychiatric settings. The similar kinds of complaints are brought to a dermatological clinic, where patients with skin problems complain of depressed moods. These kinds of cases are the classic examples of psycho-dermatological phenomenon,¹ which is a sub-branch of psychosomatic medicine.² The effects of behavioral, social, and psychological factors on the bodily processes and their relationship with each other are studied in psychosomatic medicine.² In this review article, we emphasize on psycho-dermatological relationship between psoriasis and major depression.

Any disorder that involves an interaction between the brain and the skin is classified as a psycho-dermatological disorder. Three common kinds of psycho-dermatological disorders have been described so far, that includes: psycho-physiologic disorders, primary psychiatric disorders, and secondary psychiatric disorders.³ The subject of the association of skin and brain is well studied in the recent past. Moreover, the relationship between depression and psoriasis is also studied in relation to psycho-dermatology. Today, we do know that psoriasis can cause major depression, its bi-directionality (depression leading to psoriasis) is not fully understood yet. The ideas that “major depression leads to psoriasis, any cutaneous damage associated with major depression that causes psoriasis, or any inflammatory markers or cytokines released in depressed patient's brain or body that can initiate psoriasis” is not much discussed. In this article we will highlight the answers to the above mentioned statements.

The mechanism of depression has been studied in depth, and its association with various neurochemicals has been suggested. Depression is known to have an effect on the integumentary system and other organ-systems, like the cardiovascular system.⁴⁻⁸ Similarly, psoriasis is a chronic, immune mediated inflammatory disease of skin that leads to red, itchy plaques (white/silver) on the skin.⁹ Naturally, having such a severe cosmetic disease can affect the patient's mental health and may lead to depression. However, it could also be a consequence of major depression, due to an immunological and a neurochemical phenomenon.¹⁰

In this review, we will discuss the association of the human brain with the human body's immune system; inflammatory mechanism involved in the pathophysiology of psoriasis, inflammation and its relationship with major depression, and how both of these conditions could be related and augment each other; possibly due to a bidirectional mechanism. We will conclude the article with the future research recommendations.

Immune System and the Brain

Heightened keratinocyte proliferation and leukocyte invasion into the uppermost layers of skin during inflammation that characterizes the disease known as psoriasis, causing the formation of physical pathology, has recently been found to be associated with psychological disorders such as depression through the mechanisms revolving the immune system.¹⁰ Statistically speaking, significant evidence in the previous decades have suggested an association between clinically diagnosed depression, or depressive factors, and skin diseases including psoriasis on multiple occasions. In a study done by Esposito et al.¹¹ on 2391 patients, depressive indicators were present in 62% of the sample size. The presence of psoriasis in individuals, and its respective severity, has also been found to be linked with increased depressive symptomatology in a study done in 2002, where psoriatic patients were found to have even higher depressive “scores” than non-psoriasis afflicted depressed patients.¹² Topping it however, Gupta et al.^{13,14} on two occasions observed that elevation in psychosocial impairment related to depression and stress strongly correlated to psoriasis morbidity and the onset of physical pathology. Reduction in psoriatic clinical morbidity due to medical or other treatment has also been linked to reduced depressive symptoms, with the converse true as well, in multiple studies.¹⁵⁻²¹ However, as with any apparent dermatological, or even non dermatological disorder for that matter, the antisocial, emotional, self-esteem lowering, anxiousness, and other factors that affect the psychological health of an individual are strong possibilities as to why depressive symptoms are effected and the data above is observed, but this does not explain the converse and this paper supports the idea that there is an even stronger connection between the immune system and the brain not yet fully explored.

Inflammatory Mechanism of Psoriasis

The presence of keratinocytes, leukocytes, T cells, macrophages, and dendritic cells and their migratory pathways towards the epidermis, the outermost layer of skin, and away from the inner layers, followed by the release of inflammatory cytokines including interleukin (IL) 1 β , and IL-6, IL-22, tumor necrosis factor- α , (TNF- α) or a type-1 cytokine profile (IL-2, interferon [IFN] γ , and TNF- α) has been observed to be the cause of psoriasis, or more specifically psoriatic lesions.^{22,23} IL-6 and other cytokines are thought to influence maturation of T cells into Th17 cells, pulling neutrophils to specified location.²⁴ IFN- γ and TNF- α levels may also be elevated from either Th1²⁵ or Th17 cells,²⁶ and further amplify

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