Assessment of Serum Brain Derived Neurotrophic Factor Level and Cognitive Functions in Psoriasis Vulgaris Patients
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Abstract
Background: Although inadequately studied in psoriasis patients, brain-derived neurotrophic factor (BDNF) has been demonstrated to have a critical role in the development of various autoimmune illnesses. Objectives: examining the relevance of serum levels of brain-derived neurotrophic factor in psoriasis patients compared to healthy controls and determining how these levels relate to cognitive abilities. Data Sources: By going through and examining the Medline databases (Pub Med and Medscape) for papers published up until 2022 that looked at the potential function of brain-derived neurotrophic factor in people with psoriasis. Study Selection: The following inclusion criteria were independently evaluated for compliance in each study: 1. Written in English and published in English. 2. Printed in journals with peer review. 3. Describe how serum concentration varies. Brain Derived Neurotrophic Factor may be related to psoriasis vulgaris, and psoriasis sufferers may have cognitive impairment as a result. Data Extraction: The following criteria were used to evaluate the quality of the study: eligibility criteria that were clearly stated, acceptable controls, sufficient information and well defined evaluation methods. To gather information on the research results we were interested in, data from each eligible study were separately abstracted using a data collecting form. Conclusion: Patients with psoriasis vulgaris have reduced serum BDNF levels, which is often accompanied with cognitive decline.

Key words: Psoriasis Vulgaris, Serum Brain Derived Neurotrophic Factor, Cognitive Functions. Reactive oxygen species (ROS) generation and pro-inflammatory cytokine exposure over an extended period of time in psoriatic patients decrease neurogenesis and synaptic plasticity, as well as neurodegenerative processes including DNA damage, neuronal death, and apoptosis, particularly in the hippocampus and prefrontal cortex, disrupt cognitive skills and increase the patient’s risk for depression [5].

1. Introduction
The most common chronic immune-mediated inflammatory illness that affects the skin and joints and is linked to abnormalities in other systems is psoriasis. About 1% of children and 3% of the world’s population are affected by it [1]. The neurotrophin known as brain derived neurotrophic factor (BDNF) aids in the formation, survival and function of neurons. It has a significant impact on memory and cognition [2]. BDNF affects keratinocyte proliferation and death in psoriasis via the tyrosine kinase B (TrkB) receptor, which is also its primary receptor. It causes keratinocyte death but has little effect on basal keratinocytes that accelerate psoriatic transit [3]. Psychological stress, which is worsened in psoriatic patients, lowers BDNF levels through activating the sympathetic-adrenal -medullary axis and hypothalamic-pituitary-adrenal axis, which raise cortisol and neuroinflammatory cytokines and lower BDNF levels, respectively [4].

2. Materials and methods
Data Sources: A search of the Medline databases (Pub Med and Medscape) turned up the literature on the alleged association between the blood level of BDNF and psoriasis vulgaris and its connection to the severity of the illness and related comorbidities as cognitive loss up to 2022.

Study Selection: Studies were picked after going through a strict, impartial and open selection procedure. If they met the requirements listed below, they were
considered:
1. Published and written in the English language. 2. Appearing in journals that follow a rigorous peer-review procedure. 3. Describe the connection between psoriasis vulgaris and serum brain-derived neurotrophic factor and how it could be related to cognitive impairment in psoriasis sufferers.

Data Extraction: If a research study did not fit the inclusion criteria, it was excluded. The study’s quality was determined by many different criteria, including ethical approval, eligibility requirements, controls, information, and well specified assessment methods. A data collecting form was used to independently extract data from each eligible qualifying research in order to acquire information pertinent to the results of our interested investigation.

3. Review of Literature: Psoriasis
Psoriasis is a prevalent immune-mediated illness that affects the skin and joints in those with certain genetic predispositions [6]. Sharply defined, crimson plaques with adhering silvery white scales and a propensity for symmetrical distribution over the body are features of psoriasis [7]. Patients with psoriasis have a worse quality of life than healthy people and are more likely to experience sadness and suicidal thoughts. As a consequence, psoriasis has a long-term negative impact on people’s physical, mental health and finances as well as on society as a whole [8].

Both men and women may have psoriasis. Psoriasis is more prevalent in males, according to several World Health Organization research on the condition. Psoriasis may start at any age, however it tends to occur more often in adults [9]. The many clinical forms of psoriasis include psoriasis vulgaris, which affects between 85% and 90% of psoriatic individuals and is the most common form [10].

Etiopathogenesis of psoriasis
When specific environmental stimuli are exposed, a dysregulated immune response results in psoriasis in genetically susceptible people [11]. Infections, stress, medications, smoking and endocrine variables top the list of psoriasis risk factors [12]. Psoriasis has a diverse, complicated and yet poorly understood aetiology. Through a genetically programmed disorder of dysregulated inflammation, psoriasis is fueled and perpetuated by a number of immune system cells [13]. The cytokines generated by immune cells and the immunological interactions between keratinocytes, dendritic cells, T cells, neutrophils and other immune cells are believed to have a role in the beginning of the cutaneous inflammation that is typical of psoriasis [14]. The persistent inflammation that causes unchecked keratinocyte growth and defective differentiation is the primary pathophysiology of psoriasis [13]. The maturation of myeloid dendritic cells (mDCs) and the production of TNF, IL-12, and IL-23 are encouraged by the activation of plasmacytoid dendritic cells (pDCs), which then triggers the activation of Th (T helper) 1 and Th17 and the release of inflammatory cytokines like TNF, IL-17, IL-21 and IL-22. When these cytokines, particularly IL-17, activate keratinocytes, they create antimicrobial peptides, cytokines, and chemokines that increase inflammation [15].

Psoriasis Clinical Classification
Psoriasis manifests itself clinically in a variety of ways. However, before exhibiting further symptoms such joint pain or swelling, the majority of psoriatic individuals first show cutaneous involvement. Although psoriasis vulgaris may often be diagnosed only based on clinical indicators, further research, such as a histological evaluation of a skin sample, may be beneficial [16].

Psoriasis vulgaris (PV)
The most typical clinical manifestation in psoriasis sufferers is psoriasis vulgaris, also known as chronic stationary psoriasis or plaque-type psoriasis. It often manifests as erythematous, pruritic plaques with distinct borders that are covered with silvery-white scales. When these scales are removed, small punctate bleeding points are revealed. These bleeding points are caused by larger dermal capillaries bleeding after the suprapapillary epithelium that covered them was removed. The "Auspitz sign" is the name of this sign. The elbows, knees, scalp, umbilicus, and lumbar region are the areas where lesions most often develop [17].
Guttate psoriasis
This kind of psoriasis, which is the second most prevalent, often begins at a young age (childhood to young adulthood). Small, round, sometimes scaly papules develop on the arms, legs and chest, with uncommon instances also affecting the scalp, cheeks and ears. A streptococcal infection, usually streptococcal pharyngitis, often causes guttate psoriasis. Although the condition is self-limiting, some afflicted people may develop a more chronic form of plaque psoriasis [18].

Psoriasis with flexural inversion
Smooth, irritated skin patches are the hallmark of inverse psoriasis. These patches commonly affect skin folds, particularly those in the groin, axillae, the intergluteal gap between the buttocks and the inframammary fold beneath the breasts. This unique kind of psoriasis is considered to be triggered by warmth, infection, and trauma [19]. Contrary to plaque psoriasis, the lesions’ surfaces tend to be moist, smooth and glossy, and white scales are often minor or nonexistent. Itching, discomfort from sweating and pain are typically seen as a consequence of recurrent superficial erosions and maceration [20].

Erythrodermic psoriasis
Over 90% of the whole body's surface is erythematous and inflamed in this severe disease. Any kind of psoriasis may develop erythroderma, which can be very painful, swollen and itchy. It typically results from the worsening of unstable plaque psoriasis, particularly when systemic glucocorticoids are abruptly stopped. It needs immediate medical attention [21].

Pustular psoriasis
Multiple, merging sterile pustules are the defining feature of pustular psoriasis. Both localised and widespread pustular psoriasis exist. Psoriasis pustulosa palmoplantaris and acrodermatitis continua of Hallopeau are two separate localised manifestations that both affect the hands and foot. Acrodermatitis continua of Hallopeau affects the nail apparatus and is more distantly distributed at the tips of fingers and toes than psoriasis pustulosa palmoplantaris, which is limited to the palms and soles [22]. Systemic symptoms are often evident in generalised pustular psoriasis, which has an acute and quickly progressing course marked by widespread redness and subcorneal pustules [23].

Nail Psoriasis
About 45% of individuals with skin psoriasis get nail involvement, while 90% of patients with psoriatic arthritis experience nail involvement at some point in their lives. Psoriasis of the nail may include the nail bed, the matrix, or both. These modifications include nail pitting, nail whitening, capillary splinter bleeding, thickening in the nail beneath the nail (subungual hyperkeratosis), yellow-reddish colouring of the nails (oil drop or salmon spot), nail loosening and detachment (onycholysis) and nail disintegration. The most common symptoms are pits, which are tiny, strongly defined depressions on the nail surface. Psoriasis is said to be present if a nail has ten pits or more than fifty pits on all of them [24].

Psoriatic arthritis
According to one definition, psoriatic arthritis is "an inflammatory arthritis that develops throughout the course of psoriasis and is distinguished by negative rheumatoid factor. According to estimates, up to 30% of people with psoriasis also have psoriatic arthritis. Psoriatic arthritis patients often have inflammatory joint pain and erythema across the afflicted joint, along with morning stiffness that lasts for more than 45 minutes and gets better with exercise but becomes worse with rest. Any joint may be impacted, although fingers and toes are the most often affected. Dactylitis, a swelling of the fingers and toes that resembles a sausage, may result from this. Hips, knees, the spine (spondylitis) and the sacroiliac joint (sacroilitis) may also be affected by psoriatic arthritis [25].

Evaluation of Psoriasis Intensity
The severity of psoriasis may be assessed using a variety of measures. The most used measuring device for determining the severity of psoriasis is the Psoriasis Area Severity Index (PASI). PASI generates a single score between 0 (no disease) to 72 by combining the evaluation of the area
affected and the severity of the lesions (maximal disease). In order to evaluate the effectiveness of retinoid therapy in patients with persistent plaque-type psoriasis, Fredriksson and Pettersson created the score in 1978. The four anatomical areas of the head, trunk, upper and lower extremities are used to determine the severity and extent of the psoriatic plaques independently [26]. The words mild, moderate and severe are then used to describe PASI scores. A PASI score of 5 to 10 generally denotes moderate illness, while a score of 10 or more denotes severe disease. The current standard for the majority of psoriasis clinical trials is a 75% decrease in the PASI score (PASI 75) and the FDA has authorised novel psoriasis medicines only if they meet this standard [27].

Brain Derived Neurotrophic Factor (BDNF)
BDNF is a protein that belongs to the neurotrophin family of growth factors that promotes synaptic transmission, differentiation and survival of neurons as well as the control of synaptic plasticity [28]. It is produced in cells as a precursor molecule (proBDNF), which the convertase enzyme then proteolytically cleaves to produce the mature, physiologically active form, BDNF [29].

Mechanism of BDNF activity
The tropomycin receptor kinase B (TrkB) family of tyrosine kinase receptors and the pan75 neurotrophin receptor (p75NTR) are two examples of receptors that BDNF binds to in order to function [30]. The majority of BDNF’s physiological effects depend on its ability to influence gene transcription. In actuality, genes controlled by BDNF have a role in neurogenesis, synaptic plasticity regulation, cognitive functioning, metabolism and the production of ion channel and receptor subunits [31]. BDNF and mental problems are related. It was discovered that the release of BDNF was activity-dependent. Postsynaptic BDNF signalling is involved in improving different ion channel function, transient receptor potential cation channels, sodium and potassium channels, while presynaptic BDNF signalling encourages neurotransmitter release. BDNF modulates both spontaneous and induced neuronal activity by acting at both excitatory and inhibitory synapses [32]. Its substantial potential significance in the disease pathophysiology or treatment of many mental illnesses, including as stress, anxiety, and depression, is connected to changes in BDNF levels across a variety of psychiatric disorders and having similar pathophysiological pathways [33].

Relationship between BDNF and certain dermatological diseases:
Skin conditions that manifest mentally might lead to worry, despair or embarrassment. The majority of individuals place a lot of importance on both their own and other people’s looks. Many individuals might experience major stress from even little changes in their skin’s state (such moderate acne), while others can handle receiving a diagnosis of a serious skin ailment easier [34]. Psoriasis, vitiligo, acne vulgaris, chronic eczema, acne rosacea and several other skin conditions may have an impact on a person’s mental health by altering their perception of themselves and some elements of their social lives. Psychological conditions can also arise as a result of skin conditions. However, research has shown that stress has a role in a variety of dermatological illnesses and several ideas have been put out to explain this relationship [35].

Psoriasis and BDNF
Neuropeptides and their receptors affect epidermal proliferation and apoptosis in psoriasis. BDNF affects keratinocyte growth and death via the tyrosine kinase B (TrkB) receptor, which is also its primary receptor. The psoriatic transit-amplifying subpopulation of basal keratinocytes is not affected by BDNF’s ability to trigger keratinocyte death [3]. Furthermore, psychological stress in people with psoriasis stimulates the hypothalamic-pituitary-adrenal and sympathetic-adrenal-medullary axis, boosting the production of cortisol and neuroinflammatory cytokines and reducing BDNF levels [36].

Cognitive processes in psoriasis
The higher mental processes, including as memory, attention, executive functions, visuospatial abilities, language and abstract thinking, are sometimes referred to as “cognitive functions” [37]. According to reports, long-term
potentiation (LTP) and long-term depression (LTD), which take place as cellular processes for learning and memory, depend on the secretion of BDNF. Memory tasks have received a lot of attention in studies looking at how BDNF affects cognitive function [38].

The relationship between cognitive decline and cutaneous inflammation in psoriasis
Numerous research also point to a connection between psoriasis and cognitive impairment. Mild Cognitive Impairment (MCI) rates are greater in psoriatic individuals, with the cortical thickness of the left hemisphere's parahippocampal and superior frontal gyri being greatly reduced [39]. Plaque psoriasis-related cognitive impairment is mostly shown in the memory, executive functioning, visuospatial, and attention and concentration domains [40]. Elevated levels of circulating cytokines and oxidative stress in psoriasis can increase blood-brain permeability and cause brain inflammation, which impairs neurogenesis and synaptic plasticity and triggers neurodegenerative processes such as DNA damage, neuronal death and apoptosis, particularly in the hippocampus and prefrontal cortex. As a result of these alterations, cognitive impairment develops [41]. Pro-inflammatory cytokines and psychological stress, which are worsened in psoriasis patients, also activate the hypothalamic-pituitary-adrenal (HPA) axis on all levels, raising cortisol and decreasing BDNF levels, further impairing cognitive abilities of the brain [42].

4. Conclusion:
According to the study's findings, people with psoriasis had reduced blood levels of BDNF, which is linked to the severity of their condition and cognitive deterioration.

5. References


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