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Affective immunology: where emotions and the immune response converge

Fulvio D'Acquisto, MSc, MRes, PhD

Affect and emotion are defined as "an essential part of the process of an organism's interaction with stimuli." Similar to affect, the immune response is the "tool" the body uses to interact with the external environment. Thanks to the emotional and immunological response, we learn to distinguish between what we like and what we do not like, to counteract a broad range of challenges, and to adjust to the environment we are living in. Recent compelling evidence has shown that the emotional and immunological systems share more than a similarity of functions. This review article will discuss the crosstalk between these two systems and the need for a new scientific area of research called affective immunology. Research in this field will allow a better understanding and appreciation of the immunological basis of mental disorders and the emotional side of immune diseases.

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The emotional-immune response continuum: the case for research in affective immunology

Studies over the last few decades have provided sufficient evidence for similarities and overlaps between the immune and emotional responses. The majority of living beings use both systems to adjust dynamically to the ever-changing conditions of the external environment. Both systems can either be protective for the body if kept under control or detrimental to it when they are in disarray. Despite the vast body of knowledge we have gathered on the links between these two systems, there have been very few attempts to move this area of research from bench to bedside.[1-9] This might be due to many causes, including the perceived impression that the world of immunology and that of psychology or psychiatry are completely different, if not polar opposites.

One of the main aims of this review is to help overcome this skepticism and to highlight the importance of these similarities in clinical settings. Indeed, I firmly believe that a deeper understanding of the cellular and molecular links between the emotional and immuno-

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logical systems can lead to significant advances in translational research. I call this new field of research "affective immunology" (www.affectiveimmunology.com) to distinguish it from the broader field of psychoneuroimmunology and to specifically connect the immune response to emotions and behavior and vice versa.

What is affective immunology and what are its aims? First and foremost, affective immunology is a framework of research based on two fundamental assumptions: (i) the immune and emotional systems mirror each other; (ii) both the immunological and emotional responses are dynamic and continuously changing. The first assumption is based on a large body of both clinical and experimental evidence showing an increased incidence of emotional disorders in patients suffering from immune diseases[1,10-14] and an increased susceptibility to immune diseases in patients suffering from mental disorders.[15-18] These links and connections have been extensively discussed in several review articles,[1-3,6,18-22] including our own.[23-25] The second assumption is based on new and emerging ideas that both the emotional and immune systems are highly "plastic."[26-33] The term plasticity has been used to indicate the ability to change and adjust continuously depending on the external factors or living conditions.

From the translational point of view, plasticity is a very interesting feature of this area of research. In fact, unlike genetic mutations or inherited predisposition to diseases that cannot be modified, we can exploit plasticity to bring about therapeutic changes in a relatively easy way. Adopting a healthier diet,[34,35] developing a stable emotional intelligence,[36-38] improving one's socioeconomic conditions,[39] and ceasing unhealthy habits such as drinking or smoking[40] have all been reported to be beneficial for both the emotional and immunological responses. However, how all these diverse approaches specifically exert their therapeutic effects is far from being clear.[23]

This article will provide a brief overview of the complexity (and fascination) of the crosstalk between the emotional and immunological systems. More specifically, the aim is to show how the reductionist approach of just linking "being happy" or "being stressed" with "feeling well" or "feeling sick," is neither useful nor scientifically robust. It will begin with a discussion on how established and subject-specific factors, such as personality type or certain immune repertoires, can predispose to the development of immune and emotional disorders. Next, we will try to convince the reader that the duration of what one could call an immunological or emotional challenge is a key factor in determining its impact on the emotional or immunological response. Last but not least, the translational potential of these findings will be discussed, hoping that this will inspire future scientists to see the therapeutic promise of affective immunology.

Carl Jung and Sigmund Freud were immunologists, but they did not know it

The beginning of the 19th century saw a great many changes in society worldwide, with some aspects being catastrophic and others revolutionary and life changing. Many unique personalities populated this historical period. In the field of psychology, Sigmund Freud and Carl Gustav Jung emerged as the founders of new landmark theories that changed the way we think about ourselves in the context of society. For Sigmund Freud, daily living was the result of a compromise between what one really wants and desires (the id) and what society expects from us (the superego).[41] Carl Jung was very interested in patterns of daily living, and he defined two different attitudes called extroversion and introversion.[42] The focus of extroverted personalities is mainly "the external object," eg, the outside worlds. Conversely, introverted personalities show as an attitude characterized by a "focus on one's inner psychic activity."[43]

Translating these ideas into the field of immunology, one would say that innate immune cells are "extroverted," as they are always looking out for something new coming from the outside world and continuously engage with the external environment. Macrophages patrol tissues or organs, and monocytes and neutrophils quickly migrate to the site of infection during inflammation. Adaptive immune cells have an "introverted personality" because of their increased concern about creating an inner experience of life events, especially if they have been deleterious for the host. This is what immunologists call immunological memory.[44] Innate and adaptive immune cells both work toward trying to adjust the body to accommodate the requests of the external (the superego) and the internal (the id) environments.

If immune cells have different "personalities" just like human beings do, one might wonder if there is a correlation between psychological and immunological personality. A recent meta-analysis investigated whether the five basic personality traits—often referred to as

the "Big 5" personality traits[45] (openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism)—have specific immunological features or defined susceptibility to immune disorders. The study has shown a consistent association between conscientiousness and a reduced inflammatory response, as judged by the lower level of C-reactive protein (CRP) in subjects with this personality trait.[46] Ground-breaking studies by Steve Cole and colleagues have further supported this concept and shown a specific association between the Big 5 and unique patterns of gene expression in whole blood. Consistent with the other investigations, the study by Cole and colleagues showed that conscientiousness was associated with a reduced expression of proinflammatory factors.[47]

Besides the evidence provided by these studies, the idea that certain emotional traits are correlated with specific immune responses should come as no surprise. In fact, the two systems develop almost side by side, and when one becomes defective, the other one often does the same; ie, one mirrors the other, as mentioned above. If we just focus on the development of immunological and emotional competence, it is well known that both systems are subjected to a great deal of changes during childhood and until adulthood.[48-50] Both systems learn to adjust to challenges of the external environment through vaccinations (lessons for the immune system) or through the development of a healthy emotional intelligence (lessons for the emotional system).[51] Looking at the other side of the coin, eg, the dysfunctions rather than the development, both immune and emotional dysfunctions are known to have a high incidence in the age range from 30 to 50. Autoimmune diseases, such as rheumatoid arthritis, peak between 30 and 55[52]; Sjögren syndrome is more prevalent in subjects aged 45 to 60[53]; and patients suffering from multiple sclerosis usually develop symptoms when they are between 20 and 40 years old.[54] In a similar way, the highest incidence for the two main classes of mental diseases, namely anxiety disorders and mood disorders, occurs in the populations aged between 25 to 53 and 25 to 45, respectively.[55]

Acute and chronic emotional disturbances and their impact on the immune system

In the previous paragraphs, some evidence has been provided for a high degree of similarity between the emotional and immune systems, both in healthy and diseased conditions. What are the implications of these similarities, and why should we care about them? The answer to these questions should be readily clear the moment we imagine the immune and emotional responses as two connected reservoirs in equilibrium with each other (*Figure 1*). In normal or "healthy" conditions, challenges of different origins, such as pathogens or emotional traumas, are buffered in an equal proportion by the emotional and immunological systems. One classical example of this is when an infection becomes systemic. The body activates the fever response, which helps the immune system to clear the pathogen.[56] In parallel to this, the host also experiences the sickness response,[57] eg, "a coordinated set of adaptive behavioral changes" featured by "lethargy, depression, anxiety, malaise, loss of appetite, sleepiness, hyperalgesia." The combined action of the emotional and immunological reactions induced

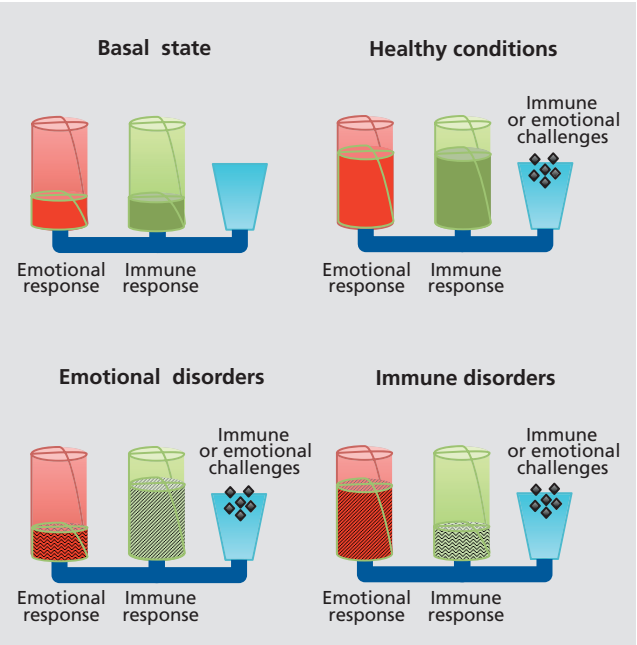

Figure 1. Schematic representation of the link between the emotional and immunological systems in healthy and diseased conditions. In a normal basal state (top left panel), the emotional and immunological responses are linked with each other in equilibrium. In healthy conditions (top right panel), pathogens of different nature, changes in environmental conditions, and significant life events prompt an adaptive response that helps the host deal with these challenges. In patients suffering from emotional (bottom left panel) or immunological (bottom right panel) disorders, the same challenges cause an exacerbated or dysfunctional compensatory immune or emotional response, respectively.

by the infection has the ultimate aim of stopping the host from increasing the chances of worsening his/her condition. This is achieved by limiting the host's activity and interaction with other living beings, thus limiting exposure to potential further infection.

What happens when the system is not in equilibrium and either the immunological or emotional response becomes dysfunctional? Several factors should be taken into consideration when answering this question, the first of which being the duration of the emotional "challenge" or immunological stimulus. When we consider emotional stimuli of short duration, for example, acute, short-term psychological stress, studies have shown that these cause a selective and timely orchestrated immune response characterized by an increase in natural killer (NK) cells in the circulation.[58-60] Downregulation of signaling sensors of the innate immune system, such as Toll-like receptor pathways, has also been reported.[61] These effects seem to be linked to the release of catecholamines and their effect on leukocytosis.[60,62-64]

A number of studies have further explored the effects of acute stress on the mobilization of NK cells and have revealed that other similar types of cells, such as $CD56^+$ NK T cells[65] and γδ T cells,[66,67] also respond to this stimulus. This is a rather interesting observation considering that these cells belong to a relatively minor category of immune cells called "unconventional" T cells.[68] Their name derives from the fact that they are not considered adaptive immune cells recognizing a specific antigen, but are more like innate cells recognizing patterns of antigens. Indeed, unconventional T cells react quite quickly to stimulation[68] and recognize nonspecific antigens, such as lipids, small-molecule metabolites, and modified peptides. Thus, it seems that the immune system is capable of distinguishing between acute stress and classical infectious pathogens by activating a specific class of immune cells. In addition, the recruitment of unconventional T cells in circulation by acute stress seems to suggest that these events might trigger the generation of antigenic small molecules, the nature of which it is still to be determined. This is a fascinating hypothesis, as the identification of such antigens would make conceivable the creation of a vaccine for people at high risk of developing emotional disorders, something that has already been suggested.[69,70]

Do acute positive emotions exert an immunomodulatory effect through NK and unconventional T cells? In studies that have considered mirthful laughter to be an acute positive emotional stimulus, it is interesting to note that such a stimulus did not increase the number of these types of cells but rather improved their biological activity.[71-74] Indeed, NK cells of healthy subjects that have watched humor videos for 1 hour showed a significant increase in the killing activity of these cells 12 hours after exposure to the video.[75] Laughing or positive humor is not the only effective stimulus for NK cells. Indeed, healthy subjects asked to watch a film featuring their favorite person, such as a love interest or favorite actor/actress (positive film), showed similar increased NK-cell activity to those who had been "treated" with an emotionally neutral film (control film).[76] In another study, volunteers were asked to follow a mindfulness-based stress reduction (MBSR) program for 8 weeks (20 to 30 minutes of meditation a day at home, 6 days a week). Most strikingly, only those subjects reporting an improvement in their emotional well-being showed an increased NK cytotoxic activity, whereas such changes were not observed in those reporting no improvement .[77]

What happens in chronic conditions? For example, what happens if the emotional and immunological challenges are present for a long period of time or have become persistent? The scientific literature in this field is vast and expands to other areas of research, including pain,[78] neurodegeneration,[79] and vascular diseases.[80] These studies are difficult to analyze, as it is challenging to establish if the activation of the immune system, for instance, is the actual driver and cause of disease or the result of the emotional response being elicited. If we just focus on cardiovascular diseases, for instance, there is now clear evidence that pathologies like atherosclerosis and even stroke have an immunological and emotional basis.[81-83] Indeed, in an elegant commentary by Pariante and Mondelli on a named series entitled "*Psychological Risk Factors and Immune System Involvement in Cardiovascular Disease*," the authors highlighted how there is now enough scientific evidence "to put an end to an era in which the heart and the mind were considered to be separate entities in which the responses of one system did not affect the other."[84] As one would expect, inflammation and activation of the immune response were the recurrent themes among all the studies included in the series. Putting all this together, it is clear that from an experimental and therapeutic point of view, understanding how chronic dysfunctions of the immune or emotional system influence another system is far from being simple. Is it that chronic stress causes

depression, which then causes inflammation, which is in turn responsible for the increased risk of cardiovascular disorders or is it that constant inflammation causes depression and ultimately an increased risk of developing cardiovascular disease? Where is the beginning and where the end of this vicious circle?

A possible solution to this dilemma might come from a slight change of approach. Most of the studies currently in the literature focus on the effects of chronic negative emotions on the immune system. These can range from divorce and marital problems[85,86] to bereavement[87-89] and loneliness.[39,90,91] Surprisingly, however, very little has been published on the effect that positive emotional states have on the immune response. Of course, one might argue that it is easier to study disease conditions and challenging to study "wellness," especially if there is no such condition as "being well"; indeed, there are almost no biomarkers that would indicate whether someone has a strong immune resilience or competence. At best, scientists have so far measured a reduction in known biomarkers of "negative emotional states," including cortisol, catecholamine, and various cytokines, such as tumor necrosis factor α (TNF-α), interleukin (IL)-1β and IL-6. Knowing the gene signature of positive emotional states could be beneficial from several points of view. Firstly, it would provide new therapeutic avenues to explore, aiming to improve the immunological state of patients suffering from chronic mental disorders. Secondly, it would allow us to assess whether a dysfunction in these pathways could be a leading cause behind the cascade of complications that occur later, for example, immune defects and associated comorbidities, such as cardiovascular disorders and neurodegenerative diseases.

We tried this approach in two of our recent studies where we "administered" a positive emotional state to mice for 2 weeks. Mice were either subjected to a daily session of 1 hour of massage-like stroking[92] or housed in an enriched environment.[93] Both experimental systems have been described to improve the welfare of experimental animals[94-99] and can be considered as an artificial experimental surrogate of caressing or of changing your living conditions (such as during holidays for instance) in humans. Our results have shown that both treatments have a significant impact on the immune system. First, stroking caused a marked reduction in the noradrenergic tone of lymphoid organs. Noradrenaline acts as an immunosuppressant to the immune system, and the reduction in its levels in the thymus caused a significant increase in the number of T cells in circulation. Consequently, stroked mice showed an improved response to the immunosuppressive effects of exogenously administered hydrocortisone, providing experimental evidence for an improved immune resilience.

A similar finding was observed with mice housed in the enriched environment. Microarray analysis of CD4 T cells showed a discrete and unique pattern of genes that were specifically modulated in enriched cells. Most interestingly, these genes included the following: *SOCS3*, a member of the suppressor of cytokine signaling family that regulates $CD8^+$ T-cell proliferation through inhibition of IL-6 and IL-27; several regulators of $CD4^+$ $CD25^-$ T-cell and regulatory T-cell (Treg) differentiation; *Nr4a2* (nuclear receptor subfamily 4, group A, member 2); and *Trib1* (tribbles pseudokinase 1). *Trib1* acts upon Foxp3 (forkhead box P3; also known as scurfin) cobinding with the transcription factor to enhance its Treg-promoting function. Most strikingly, enriched T cells acquired a unique phenotype during differentiation in effector cells and produced higher levels of IL-10 and IL-17 than did CD4 T cells of mice housed in standard conditions. This new phenotype has been called Th17reg, and it has been proposed to play a key role in the resolution of inflammation,[100] eg, the active process whereby the immune system "shuts itself up" and turns down the inflammatory response.[101] Although the validity of these observations needs to be verified in vivo and in humans, these results suggest that improving living conditions is translated at the level of the immune system into an increased ability to mount an effective and protective immune response.

Acute and chronic immunological disturbances and their impact on the emotional response

Very little is known about the effects of transient or acute dysfunction of the immune system and the effect on emotional well-being. Most of the data available in this respect concern the effects of the acute administration of immunosuppressant drugs. Studies have indeed shown that the therapeutic immunosuppression brought about by calcineurin inhibitors is often limited by the side effects that these drugs have on the emotional response.[102] These effects have been especially noted in patients subjected to transplantations and undergoing cycles of immunosuppressive pharmacologi-

cal therapies. Indeed, the depressive-like behavior of solid-organ recipients affects up to 60% of this population and is independently associated with both mortality and de novo malignancy after transplantation.[103]

Unlike acute immune suppression, several studies in experimental animals have shown that chronic defects in the immune system have a dramatic impact on the emotional response. Immunodeficient mice, such as severe combined immunodeficiency (SCID) mice or recombinase-activating gene (RAG)-1$^{-/-}$ mice, have been shown to have an impaired learning and memory,[104] as well as an increased basal level of anxiety-like behavior.[105] Microarray analysis of the gene expression profile of the whole brain of RAG-1$^{-/-}$ mice showed a significant difference from that of the wild-type control. Most of the genes correlated with neurodegeneration or emotional disorders. Most interestingly, these changes were partially but significantly reversed in OT-II/RAG-1$^{-/-}$ mice, eg, mice that selectively had CD4^{+} but not CD8^{+} T cells, thus suggesting that CD4^{+} T cells exert a homeostatic control over the correct tuning of genes in the brain.[105] Along these lines, in another study performed in RAG-2$^{-/-}$ mice (immunocompromised mice similar to RAG-1$^{-/-}$), the absence of adaptive immune cells was associated with emotional deficits during inflammation. Indeed, these authors also suggested that the depressive states associated with several diseases might be mediated, at least in part, by an impaired lymphocyte response.

The mechanisms behind these effects are fascinating. Seminal work by Jonathan Kipnis and colleagues has revealed functional lymphatic vessels lining the dural sinuses that express all of the molecular hallmarks of lymphatic endothelial cells. These vessels are able to provide brain access both to fluid and immune cells from the cerebrospinal fluid.[106] The discovery of these "T-cell gateways to the brain" has allowed the same researcher to show that meningeal T cells produce interferon γ as a key mediator that regulates social behavior.[107] These findings are consistent with previous research in humans that has shown that eudaimonic well-being is associated with a decreased expression of proinflammatory genes and increased expression of genes involved in antibody synthesis and type I interferon response.[108]

Several human studies have confirmed the link between a state of immunosuppression and the development of mental disorders. The most common condition that can be taken as an example is acquired immunodeficiency syndrome (AIDS).[109,110] Most interestingly, and in line with what has been mentioned above, studies have found a correlation between lower CD4 counts and the emergence of emotional disorders in individuals who have recently acquired human immunodeficiency virus (HIV).[111] Similar increased incidence of mental disorders after or before the diagnosis of immune disease has been reported for systemic lupus erythematosus,[112] multiple sclerosis,[113,114] and rheumatoid arthritis.[115,116] However, the role of T cells or other immune cells in the regulation of the emotional response in these patients has not been explored as yet.

As I have discussed the effects of positive emotions on the immune response, one might wonder what would be the effect of an improved immune system on the emotional response. Surprisingly, little is known in the clinic about the potential of boosting the immune system to improve the emotional well-being of patients suffering from immune diseases. This is probably linked to the fact that we do not really know what the best approaches are for improving the fitness and resilience of the immune system, let alone their postulated effects on the emotional response. Yet, there is some indirect evidence that supports this idea. In line with our investigation on mice, studies on both children and adults with HIV have shown that massage therapy can increase the blood cell count of CD4^{+} cells and result in an improved emotional state.[117-120] There are other ways to increase the number of T cells in the body. One such example is the administration of IL-7, a cytokine that enhances CD4^{+} T-cell numbers. Studies on experimental models of HIV infections, such as simian immunodeficiency virus (SIV)-infected monkeys, have shown that like massage, IL-7 is effective in increasing the number of CD4^{+} T cells in these animals.[121] It would be interesting to investigate if such therapy also improves emotional state and whether this approach can be used in humans. This is an interesting idea considering that recent studies have shown a correlation between major depressive disorder and lower levels of IL-7.[122]

Perspectives

Where do we go from here? The translational value of research in the field of affective immunology is solid enough to justify new clinical trials for combined therapies targeting the emotional and immunological sys-

tems. These will undoubtedly be a great opportunity to find new therapeutic weapons for psychiatrists, rheumatologists, and clinicians dealing with immune and emotional disorders. However, this would also be a unique opportunity for basic scientists, as understanding the mechanisms by which this combined approach works would significantly shift the way we currently look at immune and emotional disorders.

Regarding the immune and inflammatory response, the biggest challenge for the future is to understand how different life events can permanently "mark" immune cells and make them more prone to develop an exacerbated immune response.[123-125] Research in this field should aim at systematically dissecting how different social and emotional conditions specifically influence the immune system. As explored in this article, it is indeed very likely that different adverse life events—eg, social isolation, physical abuse, and bereavement—might have their own "gene signature" and hence specific effects on the immune system.

Regarding emotional disorders, more studies are needed to explore what I would call the "peripheral control of emotional behavior." The advancement of technologies for the study of brain functions, such as the ever more popular functional magnetic resonance imaging (fMRI),[126,127] has helped the field of neuroscience expand exponentially in a very short period. And yet, whereas an enormous number of studies has tried to establish areas of the brain that correlate to specific emotions or mental disorders, evidence is emerging that the gut is an essential organ in the control of emotional behavior.[128-130] I have provided a few examples of how immune cells regulate emotional behavior. However, there are other examples of cells or therapies that can act as emotional modulators by changing, for instance, the composition of blood. One such example is erythropoietin—the hormone that stimulates the production of red blood cells; erythropoietin is a novel treatment for a wide range of mental disorders from depression to cognitive dysfunctions.[131-133] Similarly, it would be interesting to test the idea that changing blood composition by altering the number of specific immune cells might provide an alternative way to treat emotional disorders or dysfunctional personalities.

Besides all these considerations for the future, I think that establishing the field of affective immunology might be useful for reevaluating a large number of failed clinical trials for new therapies for immune and emotional disorders. Despite the scientific literature that has been cited in this and other articles, there are no trials for immunomodulatory drugs that take into consideration the emotional state of the enrolled patients. Similarly, there are no trials for mental disorders that assess the immune repertoire of recruited patients. Therefore, one might wonder if those trials that have failed could have had an entirely different outcome if the participants were stratified according to their social and economical conditions, their personality, emotional well-being, or even blood type. There is indeed recent evidence suggesting a correlation between the ABO blood group and personality traits.[134]

Regardless of the validity of the hypothesis and ideas presented in this article, I hope that the readers of *Dialogues in Clinical Neuroscience* will be convinced that there is a need to look at immune and emotional diseases in a different way. This new approach would consider the "whole" of the patient, from his/her immune phenotype to his/her personality, environment, and life-style, essential in order to prevent basic experimental scientists and clinicians ending up like the old blind men in the Jain parable[135] below (reproduced, in slightly modified form, courtesy of Jain World).

> Once upon a time, there lived six blind men in a village. One day the villagers told them, "Hey, there is an elephant in the village today."
>
> They had no idea what an elephant was. They decided, "Even though we would not be able to see it, let us go and feel it anyway." All of them went to where the elephant was. Every one of them touched the elephant.
>
> "Hey, the elephant is a pillar," said the first man, who touched his leg.
>
> "Oh, no! it is like a rope," said the second man, who touched the tail.
>
> "Oh, no! it is like a thick branch of a tree," said the third man, who touched the trunk of the elephant.
>
> "It is like a big hand fan" said the fourth man, who touched the ear of the elephant.
>
> "It is like a huge wall," said the fifth man, who touched the belly of the elephant.
>
> "It is like a solid pipe," Said the sixth man, who touched the tusk of the elephant.
>
> They began to argue about the elephant and every one of them insisted that he was right. It looked as if they were getting agitated. A wise man was passing by and he saw this. He stopped and asked them, "What is the matter?" They

said, "We cannot agree to what the elephant is like." Each one of them told what he thought the elephant was like. The wise man calmly explained to them, "All of you are right. The reason every one of you is telling it differently because each one of you touched a different part of the elephant. So, actually the elephant has all the features that each of you mentioned." ❑

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La inmunología afectiva: la convergencia de las emociones y de la respuesta inmune

Afecto y emoción son definidos como "una parte esencial del proceso de interacción de un organismo con un estímulo". Similar al afecto, la respuesta inmune es la "herramienta" que emplea el cuerpo para interactuar con el ambiente externo. Gracias a la respuesta emocional e inmune, aprendemos a distinguir entre lo que queremos y no queremos, a contrarrestar una amplia gama de desafíos, y a adaptarnos con el ambiente donde estamos viviendo. Evidencias recientes y convincentes han mostrado que los sistemas emocional e inmunológico comparten más de una semejanza de funciones. Este artículo de revisión discutirá las alteraciones de la comunicación entre estos sistemas y la necesidad de una nueva área de investigación científica denominada inmunología afectiva. La investigación en este campo permitirá una mejor comprensión y apreciación de las bases inmunológicas de los trastornos mentales y del aspecto emocional de las enfermedades inmunes.

L'immunologie affective : la convergence des émotions et de la réponse immunitaire

L'affect et l'émotion se définissent comme « une part essentielle du processus d'interaction d'un organisme avec les stimuli ». Similaire à l'affect, la réponse immunitaire est « l'outil » utilisé par le corps pour interagir avec l'environnement extérieur. Grâce aux réponses émotionnelle et immunologique, nous apprenons à distinguer ce que nous aimons de ce que nous n'aimons pas, pour affronter un large éventail de défis, et pour nous adapter à l'environnement dans lequel nous vivons. Des données récentes ont montré que les systèmes émotionnels et immunologiques partagent plus qu'une similarité de fonctions. Cet article de synthèse analyse les interactions entre ces deux systèmes et la nécessité de définir un nouveau domaine de recherche appelé immunologie affective. La recherche dans ce domaine permettra une meilleure compréhension et une meilleure appréciation de la base immunologique des troubles mentaux et du côté émotionnel des maladies immunitaires.