Impacts of Immune System in an Experimental Social Behavior Model: Review Article

Amal M. Mahfoz*

Department of Pharmacology, Faculty of Pharmacy, Modern University for Technology and Information, Cairo, Egypt

*Corresponding author: Amal M. Mahfoz, Department of Pharmacology, Faculty of Pharmacy, Modern University for Technology and Information, Cairo, Egypt. Tel. +201064794983
Email address: mahfozamal@gmail.com

Submitted on: 17-03-2020; Revised on: 27-04-2020; Accepted on: 15-05-2020

To cite this article: Mahfoz, A. M. Impacts of Immune System in an Experimental Social behavior Model: Review Article. J. Adv. Pharm. Res. 2020, 4 (3), 72-82. DOI: 10.21608/aprh.2020.26014.1101

ABSTRACT

There is growing evidence supports the regulatory role of the immune system in neuronal function and mental health. Many studies have demonstrated the impact of the immune system in neurodegenerative disorders. There are beneficial therapeutic effects of targeting the immune system in the management of these disorders. However, there are gaps in the available knowledge and many steps are needed to move forward. Sensory contact model (SCM) is an experimental social behavior model which allows the formation of different psychopathological conditions which are originated between male mice by the repeated agonistic interactions; resemble those in human. SCM has been developed to investigate aggression and submission behaviors. It gives the chance to study the pharmacological actions of novel psychoactive drugs. The current study aims to review the possible relations between the immune system and social behavior; using the SCM as an experimental model of aggression and depression. To encourage the production of novel psychoactive drugs target the immune system and inflammatory pathways.

Keywords: Behavior; Social behavior; Sensory contact model, Immune system

INTRODUCTION

The immune system

The immune system is a complex array of organs, cells, and soluble factors that constitute a defense mechanism aiming at the preservation of integrity being charged with the ability to identify self and nonself 1. The outcomes of the functional immune system are in most times desirable, as in termination of infection, acquiring resistance against further infection and identifying new antigens such as those expressed by newly arising tumors. However, in some instances the outcomes are undesirable. When integral body tissue performs defensive and destructive abilities against its tissues; it results in autoimmune disease, transplant rejection, or hypersensitivity reactions 2.

Based on their function, organs of the immune system can be classified into:

a. Central organs (Primary lymphoid tissues): These are organs that provide the microenvironments that support the initial development of immune cells and their priming by expressing their first antigenic receptors during the process of tolerance and attaining phenotypic and functional maturity. In mammals, primary lymphoid tissues include bone marrow, where all lymphocytes, including B lymphocytes, and blood stem cells are generated; and the thymus where T lymphocytes are generated and mature 3.

http://aprh.journals.ekb.eg/
b. Peripheral organs (Secondary lymphoid tissues): These are organs that provide sites where the antigen-specific lymphocytes respond to their cognate antigens efficiently, and where proper cellular interactions occur to provide a well-regulated immune response. They include lymph nodes, spleen, mucosal-associated lymphoid tissues, and Waldeyer's ring, which in turn includes tonsils and nasal associated lymphoid tissues. Besides, there are less well-defined clusters of lymphoid and other hematopoietic cells associated with genitourinary, gastrointestinal, and respiratory tracts.

Experimental Indicators of Immunomodulation

A battery of tests was selected to serve as indicators of the immunomodulatory potential of the different immunomodulatory candidate substances. These indicators are supposed to give the primary profile of the immunomodulatory potential that might be subjected to further investigation by more specific and detailed studies.

1. Total and differential leucocyte counts

Leucocytes are concerned with many different defensive and reparative activities in the body, essentially in destroying invading antigens as well as the production and distribution of antibodies. The alterations in normal leucocyte blood pictures may provide diagnostic clues to specific diseases both benign and malignant.

The types of leucocytes enumerated in the differential count are the lymphocytes, monocytes, neutrophils, basophils, and eosinophils. The following section includes a brief description of the roles of each type and its participation in the immune system.

a. Lymphocytes

1. B lymphocytes

The defining feature of B lymphocytes is their ability to synthesize and secrete immunoglobulins. Mature B lymphocytes express immunoglobulins in two different forms. In the effector B lymphocytes lineage (called plasma cells) immunoglobulins are secreted in large amounts into their surrounding milieu. By contrast, in the resting (virgin or memory) B lymphocytes, immunoglobulins are expressed only on the cell surface, where they serve as membrane-bound receptors for specific antigens and therefore may be referred to as handicapped B cells. When activated B lymphocytes divide, some of its progeny become B lymphocytes, while the remainder differentiate into plasma cells. The memory cells enable the immune system to encounter high-affinity responses to subsequently encountered antigens in a faster and more efficient manner.

2. T lymphocytes

T lymphocytes, which mature in the thymus gland, localize in particular lymphoid tissues throughout the body such as the paracortex of lymph nodes and the periarterial lymphoid sheath in the splenic pulp. When a specific antigen is encountered in the tissues, the T lymphocytes which are programmed to recognize that particular antigen return to the specific T lymphocytes domain of the lymphoid tissue where they transform to lymphoblasts (T immunoblasts) that divide repeatedly by mitosis. Its result is the production of activated T lymphocytes which enter the circulation and migrate to the site of antigenic stimulation. These cells can split the antigen into smaller peptides display them on their surface MHC molecules to form the required ligands with T lymphocyte receptors.

3. Null (Natural Killer) cells

This is the third major class of lymphocytes. This class expresses markers of neither B nor T lymphocytes and was, therefore called the null cell population. It is now apparent that most null cells are large lymphocytes with numerous cytoplasmic granules that are able of lysing a variety of virus-infected and tumor cells without overt antigenic stimulation. As a result, they are called large granular lymphocytes or natural killer cells.

b. Monocytes

Their principal function is phagocytosis which is mediated by their surface receptors Fc fragment of immunoglobulin G. Monocytes also participate in processing antigens and presenting them to T lymphocytes in conjunction with MHC II molecules. Moreover, monocytes have a secretory function, where they produce several cytokines including interleukins (ILs) as IL-1, IL-6, IL-10, and tumor necrosis factor (TNF).

c. Neutrophils

These cells are also called polymorphonuclear (PMN) leucocytes. They can respond rapidly to chemotactic stimuli and effectively perform their main function namely to phagocytosis of the stimulating foreign particle. Neutrophils are capable of extracellular killing of other cells if coated with the proper opsonins, mainly immunoglobulin (IgG). They attach to the protruding Fc piece utilizing their Fc receptors and kill the attached cell. A well-known example is killing schistosomula in vitro.

d. Eosinophils

Eosinophils have also a phagocytic function that starts by their adhesion to post venular capillary with their adhesion receptors to the ligand on the
endothelial cells. Eosinophils also express IgG, A, D, and E receptors, and can, therefore, undertake several IgE-dependent functions including killing helmiths coated by IgE. Eosinophils are abundant at sites of immediate hypersensitivity reactions where they contribute to tissue injury and inflammation. This effect is due to their capacity to secrete several potent mediators including lipid mediators, basic proteins, and oxygen burst components including hydrogen peroxide 18.

e. Basophils

These cells have similar functions to those of mast cells. Both types have high-affinity receptors for IgE (FcεRI), therefore, avidly bind free IgE molecules. Upon interaction with specific antigens, granular contents are released, which are namely the chemical mediators of immediate hypersensitivity. Thus, these granulocytes are effector cells of IgE-mediated immediate hypersensitivity 19.

All blood cell types originate from several multipotential hematopoietic stem cells that undergo processes of proliferation and maturation in the bone marrow under the influence of cytokines 20. They include granulocyte, macrophage, and granulocyte/macrophage colony-stimulating factor (G, M, and GM-CSF, respectively); erythropoietin and thrombopoietin. Other hematopoietic cytokines that are not colony-stimulating factors include IL-3, IL-5, IL-7 and stem cell factor 21. The bone marrow also provides a microenvironment that is particularly supportive of the differentiation and maturation of B lymphocytes and natural killer cells 22,23. Therefore, B lymphocytes cannot be produced in vitro unless they are placed onto layers of bone marrow stromal cells 24. The cultured stromal cells selectively support the differentiation of hematopoietic stem cells into myeloid lineage 25 or B cell lineages, 26, 27.

Different behavioral aspects
Social behavior

It is the behavior that is directed to society, between members of the same species. In sociology, "behavior" means an activity free of social meaning, contrary to "social behavior" that has both together. Social behavior is accompanied by social actions that are directed toward others and induced a response. So, social behavior is a process of communication 28. Behavior comes in many forms; blinking, eating, reading, dancing, shooting, rioting, and warring…etc. Such social behavior towards others apprehends another as thinking, perceiving, moral, and intentional. Consider the meaning of the other's fields of expression 29.

Conflicts behavior

Tendency towards conflict is an elementary component of human nature. Conflict may arise due to competition for scarce resources. Conflict and struggle may promote human social survival by guaranteeing that the strongest survive 29. According to Marxian theory; conflict is the basic structural condition of society. It is an inherent part of human relationships and existence. Freud’s theory stated that; self-interest is the basic to human nature; however, it is managed by conscience. There is also an aggressive unconscious force that seeks expression. The social reality is dualistic; it includes forces that promote social orders and social conflicts 29. There is an organizational network between individual parties (as individuals, summaris, groups) together with their mutual relations. Besides, the task-oriented and socio-emotional relations are combined with aspects of scarce resources 30. These aspects often result in conflict situations that may harm working environment 31. Poorly handled conflict reduces productivity, and increase relations problems 32. An individual becomes emotional throughout the conflict, he loses focus on tasks and becomes less effective, which results in lack of performance 33. Sometimes organizational conflict has positive outcomes that include; better ideas; higher interest; and creativity 34. The previous study had stressed aggression as an important result of dysfunctional conflict. Excess conflicts hinder the success of a group or organization, thus resulting in less satisfaction, increase turnover rates, and decrease productivity 35. However, the optimal level of conflict enhances motivation through the creation of challenges and questions with vitality which makes the working environment interesting 36. Approximately 21% of managers’ time spends on managing conflict 37. “Conflict handling”, “conflict resolution” and “conflict management” are different concepts 38-40. The styles of handling conflict are differentiated on two basic dimensions: concern for self and concern for others (41). A combination of these two concepts results in five different specific styles of handling interpersonal conflict 38, 42; 1. Integrating: Focuses high concern for self and others. 2. Obilging: Involves withdrawal, ignoring, and low concern for self and others. 3. Dominating: High concern for self and low concern for others. 4. Compromising: Moderate concern for self and others; give and take. 5. Avoiding: Low concern for self as well as other parties.

Aggression

Aggression may be considered as a heterogeneous phenomenon as far as motivations, context, behavioral patterns of attack and presumed functions are concerned. Wilson, 1981 43 demonstrated that aggression was classified into different types with different various endocrine bases. Maternal aggression that protects the offspring from intruders is mediated by
hormonal changes during the production of offspring 44; 45. However territorial aggression, intermale aggression, and sex-related aggression are mediated by steroidal hormones and androgens 46. Other types of aggression as learned aggression and defensive aggression seem to have different underlying neuronal mechanisms 46.

Learned aggression
Social conditions requiring the expression of prolonged aggression often appear in communities (war, sports, social security). This type of aggression in humans is known as premeditated (learned) aggression 47.

In the sensory contact model (SCM); aggressive behavior is made by repeated experience of victories in regular daily agonistic interactions in male mice. The development of learned aggression in male mice is like those in humans. Positive daily fighting experience in social conflicts modifies many features of individual and social behaviors. Physiological parameters are also changed in both winners and losers 47; 48. Neurochemical records confirm the stimulation of brain dopaminergic systems and inhibition of the serotonergic system, in the winners under the effect of repeated aggression. This creates a low threshold for aggressive behavior in a weakly provoking environment. Alterations in opioidergic systems as a result of aggression abuse in male mice. Similarities in mechanisms of learned aggression in humans and animals are discovered. Understanding the brain neurochemical basis of learned aggression as well as pathological aggressiveness can be useful for pedagogics, the science of law, and Centers of rehabilitation for war participants 47.

Depression and anxiety
Stress resulted in psychoemotional negative effects in humans as anxiety, depression, and phobias. Repeated defeat in daily agonistic interactions results in dramatic changes in the social behaviors of losers, which were close to human depression regarding etiology, vulnerability to treatment, symptoms, and neurochemical changes. A significant behavioral deficit, meaninglessness, depression, anxiety, alcohol addiction, in addition to weight loss, reduction of stress reactivity, and sexual dysfunction were found also in the losers 47.

Anxiolytics or antidepressants had positive effects. Chronic social stress is considered as an important pathogenic factor, which aggravates the development of mixed depression/anxiety state in experimental animals. The study of brain neurotransmitters in the losers allowed imagining the dynamic changes in the brain serotonergic and dopaminergic systems; depending on the depth and duration of depressive disorder. The SCM is a unique experimental model since it permits the examination of neurochemical, behavioral changes, and to suggest specific pharmacological treatments. This model of anxious depression produced by social stress and permanent anxiety is the most adequate and productive one at the present time and can be used for many aims of biological psychiatry 48.

Experimental models for different types of behaviors

Sensory Contact Model (SCM):
The effects of stressful events on the development of psychopathologies have been investigated in animal studies. It was demonstrated that different types of stressors, duration, and intensity produce different responses 49; 50. The most common stressors in humans are social 51; 52. So, using the social animal conflict model has an evident advantage over other animal models that require physical stimuli as restraint, electric foot shock, food or water withdrawal, or cold exposure. Previous studies had shown that social defeat stress is an important factor that results in psychopathological impacts 52.

In the first agonistic encounter; behavioral differences often appear between dominant and subordinate animals. One animal begins to win, and the other to lose in the first fight. Successive fights usually occur more quickly, till fighting is avoided overall by the withdrawal of the subordinate. The changes between the behavior of two strangers to the behavior of dominant and subordinate can happen quickly within minutes of their first encounter. These behavioral states can persist for periods, from hours to a lifetime 51.

It was demonstrated that repetitive experience of aggression in winners is accompanied by the stimulation of the brain dopaminergic, and opioidergic systems along with inhibition of the serotonergic system 54; 55. However, repeated experience of depression by social defeats in losers results in a reduction of the activity of all these mediators 56. Therefore, the winners and losers have been found to show significant differences in emotions, motor activities, gonadal function, level of sociability, and the state of the immune system 57.

Therefore the sensory contact model is important in generating different psycho-emotional disturbances in animals. In this respect, it would be useful to outline possible applications of the proposed experimental method for detecting therapeutic and protective effects and efficacy of prospective novel psychotropic drugs 58; 59.

Locomotor activity is required for many complex behavioral tasks. Thus, it should be measured before performing any other behavioral characterization. Several aspects of locomotion could be measured, for example, response to novelty,
exploratory behavior, and locomotor response to drug treatment. It should be considered that all measures of activity are sensitive to the circadian clock. Therefore, the experiments should be performed daily at the same time 60.

Open field test (OFT) is a test used to evaluate both locomotion activity and emotionality of the animal when exposed to either square or circular open arena under standard conditions 61; 62; 63; 64. In the OFT; the situation induces anxiety behavior in rodents by two factors; 1. The animal is separated from its social group; 2. Agoraphobia; as the area is very large relative to the animals’ environment 65.

Mahfoz, 2019 48 reported that the winner partner in SCM had higher motor activity in OFT which was demonstrated by a significant increase in ambulation & grooming and a decrease in latency. The higher aggression is associated with the higher motor activity 66. Aggression contains more features of motor activity 45.

Higher aggression in winners is accompanied by higher anxiety. This was manifested by lower time spent in the open arm of the elevated plus maze (EPM) test 48. This may be due to fighting for dominance which leads to high fearfulness and anxiety and neurotransmitters imbalance 57; 67.

The EPM is a test used to measure anxiety and emotionality. It represents the natural conflict between the tendency of mice to explore a novel environment and the fear from brightly lid open places 68; 62.

Losers exhibited many behavioral changes; include low motility accompanied by a parallel reduction in DA levels which indicates the depression state of defeated mice 48. Rygula et al. (2005) 69 also reported that chronic stress in rats resulted in higher immobility in forced swimming test and low preference for a sweet solution.

Impacts of Different Behavioral Aspects on Neurotransmitters

Social information processing in the mammalian brain

Sensory information is processed in the fusiform area, accessory olfactory bulb, or superior temporal gyrus. This signal comes to be instantiated as marked or silent in a successive multimodal projection to defined fields in the temporal cortex, prefrontal cortex, and amygdala, where social status, emotion, or familiarity may be programmed. However, social attachment as pair bonding, maternal behavior, and infant attachment involves enrolment of the mesolimbic dopamine pathway together with the ventral tegmental area. In conclusion, social behavior implicates the stimulation of the neuroendocrine hypothalamus, plus the medial preoptic area, in addition to, motor and autonomic centers 76.

Other brain regions have been reported to be involved in aggression. The elimination of the temporal lobes leads to a passivity syndrome. Lesions in some brain areas as the lateral septum, olfactory bulbs, dorsal and medial raphe, medial accumbens, and amygdala increase defensiveness but didn’t affect social aggression 77; 78.

Aggression is salient stressors for both the aggressor and the victim. It is accompanied by stimulation of the mesocorticolimbic region, but not the striatal dopamine. It has been reported that targeting the D2 receptor family, may affect aggressive behavior in both animals and human patients, this suggesting that the mesocorticolimbic dopamine pathway may have significant enabling or permissive functions 79.

Aggression in winners is associated with increase brain NE and DA levels; while repeated social defeats resulted in attenuation of 5-HT; NE; and DA. This indicates the obtained physiological state in losers and winners 55.

Developments in our information about the neurobiology of pathological aggression have led to the discovery of rational pharmacological treatments for these behaviors. Many biological systems are known to be involved; such as serotonin (5HT), testosterone, opioid peptides, gamma-amino butyric acid (GABA), dopamine [DA], and Nor epinephrine [NE]80; 85. The pathological aggression is associated with low levels of the serotonin metabolite 5-hydroxy-indoleacetic acid in the cerebrospinal fluid and low blood level of serotonin 80; 83.

Moreover, others reported on a Dutch family in which a gene mutation in the monoamine oxidase enzyme (MAOA), resulting in a defect in the breakdown of DA, 5HT, and NE, was associated with markedly increased aggressive behaviors in teenagers 81.

Enhancing catecholamine function by treatment with alpha-2 adrenergic receptor antagonists’ was found to increase aggressive responses to intruders 86. Further experiments 87 in rodents revealed that tricyclics and MAO inhibitors, which increased both DA and NE activity, also enhanced aggressive behavior in these animals. In humans, the NE metabolite 3-methoxy-4- hydroxyphenylglycol correlated with a positive history of aggressive behavior 88.

Acute isolation-induc ed fighting in mice produced a striking “dose-dependent” increase in dopamine uptake in mesocortical nerve endings (synaptosomes) but no significant changes for these uptake constraints in nigrostriatal terminals 89. Moreover, the DA metabolite 3-4- dihydroxyphenylacetic acid (DOPAC) was significantly lower in muricidal rats compared to nonmuricidal animals. The hippocampus of muricidal rats (rats which killed mice)

http://aprjournals.ekb.eg/
showed significantly higher DA levels, and higher levels of the NE metabolite homovanillic acid (HVA) were found in the hippocampus of muricalid rats\(^9\). 

**Behavior and immunity**

The endocrine, immunological, and nervous ‘super-systems’ are engaged in various connections during the reaction of the body to acute or chronic stress\(^9\). This network bonds relevant ligands with their cognate receptors\(^9\). Whether or not a healthy balance of protective or damaging effects of stress responses is achieved, it is affected by the concept of allostasis\(^9\). Allostasis; is known as the adaptation of the endocrine, immune, and nervous systems to keep stability throughout psychological changes, for example unpredictable events: as social conflict, competition for resources, or predictable events: as seasonal changes\(^9\).

Neurotransmitters, neurohormones, neuropeptides, and neurotrophins stimulate a series of adaptation responses in response to stress. These changes are ranged from immunosuppression to inflammation\(^9\); 95; 96.

These reflect the multifunctional role of the immune system in the stress response. The immune system also controls the central nervous system (CNS). Inflammatory mediators and cytokines influence behavior and complex body reactions. Proinflammatory cytokines can induce sickness behavior or depressive symptoms\(^9\). Several diseases have been recognized to be aggravated by psychological stress. Such as: migraine, inflammatory bowel disease, allergic encephalomyelitis, and multiple sclerosis\(^9\).

Central hypothalamic-pituitary-adrenal (HPA) axis and corticotropin-releasing hormone (CRH) have a major role in controlling and coordinating complex responses to psychological stress\(^9\). Relevant examples for the pro-inflammatory actions of CRH had been introduced; include carrageenan-induced arthritis and aseptic inflammation\(^9\); 98.

Histamine release from mast-cells increases the expression of CRH mRNA in the hypothalamus, this activates the HPA. Moreover CRH release could be triggered by IL-1 and IL-6, both are released also from mast cells. On the other hand, CRH stimulates IL-6 release\(^9\).

In humans, positive correlations have been observed between the development of infectious episodes and depressive state\(^10\); 101; 102; 103. Chronic activation of the cytokines network (e.g., multiple sclerosis and rheumatoid arthritis) has also been correlated with a propensity to develop a depressed mood\(^10\); 105; 106. A correlation has also been shown in women between the increased liberation of cytokines occurring at childbirth and a post-partum depressive mood\(^10\); 109.

Previous studies have demonstrated that the administration of IL-2 or Interferon (IFN) induces depression symptoms in cancer patients. Besides, patients with major depression have reported a higher level of central cytokines\(^11\).

It has been demonstrated that the behavior of patients with viral or bacterial infection changes dramatically. They often feel nauseated, ignore food, and lose interest in their physical and social environments. Furthermore, they are irritated and feel depressed, they can experience mild cognitive disorders ranging from impaired attention to difficulties in remembering recent events. Despite their negative impact on well-being, these symptoms of sickness are usually ignored\(^9\).

Regarding the immunological parameters; it was reported that winners had a significant increase in lymphocytes counts; and viability \(^70\). Line et al., \((1996)\)\(^71\) reported that aggression is associated with the strong immune response which may be due to NE elevation\(^72\). However, losers have shown weaker immune response demonstrated by the reduction in lymphocytes counts, and viability\(^70\). This may be due to higher corticosterone levels in losers with depressive behavior, which is immunosuppressant, thus induced cell destruction and lymphocytopenia\(^73; 74; 75\).

It had been reported that cellular and humoral immunity is suppressed in the losers partners in SCM. This means that depression state in loser results in psychogenic immune deficiency. Therefore, the sensory contact model can be used to study the neurochemical and physiological mechanisms of immune suppression along with the possible pharmacological interventions\(^59\).

The brain is considered an immune-privileged organ. It contains immune cells, like macrophages, and dendritic cells, which present in the meninges and choroid plexus. The brain parenchymal macrophages, which known as microglial cells, are more inert as compared to other tissue macrophages; but can respond to inflammatory stimuli by pro-inflammatory cytokines and prostaglandins production\(^110\). Neuroinflammation is a significant biological event that increases the risk of major depressive episodes\(^110\).

Variables details about how the immune system can influence the brain function had been elaborated. The immune system has a vital role in neurodegeneration and the development of various psychiatric disorders. Autism may result from maternal or host autoantibodies that disrupt neurons that regulate social behavior\(^111\). Schizophrenia represents overactive immune response which results in neurotransmitters dysregulation\(^112\). Many studies have reported the impact of the immune system and inflammation

---

**http://aprh.journals.ekb.eg/**

77
pathways in neurodegeneration occurred in epilepsy. Niraula et al., 2017 have reviewed the impact of chronic stress on the aging of immune cells. He described age-related hyperresponsiveness and pro-inflammation those have been consistently associated with neurodegeneration and accelerate the aging process.

In line, Eisenberger et al. (2017) had discussed the co-regulations between inflammation, and social behavior through neural circuits that stimulates the adaptation to social environments throughout durations of sickness or stress. Acute inflammation raises threat-associated neural sensitivity to negative social experiences. However, increasing reward and motivation associated neural sensitivity toward positive social experiences like care or support during sickness. On the contrary, social behavior may similarly regulate features of inflammatory activity for preparing the body for stress situations.

Michopoulos et al., (2017) also evidenced the role of immune system activation in phobias, posttraumatic stress disorder, panic disorder, and generalized anxiety disorder. Stress or trauma exposure is associated with dysregulation of the autonomic and neuroendocrine systems; these precipitate the release of cytokines which increase symptoms severity through effects on brain circuits critical for the regulation of fear and anxiety (eg, prefrontal cortex, insula, amygdale, and hippocampus). These effects of inflammation on neurotransmitters and neural circuits are further extended in the review by Brundin et al. (2017) who reported an association between inflammatory activation and suicidal behavior reported through psychiatric disorders. On the basis of this association, they propose that biomarkers of inflammation and its downstream mediators including metabolites of the kynurenine pathway, which relate to both glutamate and serotonin and, provide a mechanism by which suicidal behavior happens. These findings suggested that the immune system affect fundamental pathways which regulates social behavior and in that way represents a critical pathway to the pathophysiology of different neuropsychiatric diseases.

CONCLUSION

On the basis of this review, it could be concluded that the immune system has a strong impact on neurons, brain function, and social behavior. Neuroinflammation is involved in many neurodegenerative disorders. Novel pharmacological treatments that target autoimmunity, anti-inflammatory, and neuroprotective strategies may have a potential impact on both developmental and neurodegenerative psychiatric disorders.

Conflict of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

REFERENCES


http://aprh.journals.ekb.eg/

http://aprh.journals.ekb.eg/


69. Rygula, R.; Nashat Abumaria; Gabriele, F'Iugge; Eberhard Fuchs; Eckart R’uther; Ursula Havemann-Reinecke. Anhedonia and motivational
93. Dantzer, R. Cytokine-induced sickness behaviour: a neuroimmune response to activation of innate

http://aprh.journals.ekb.eg/