Title: Stress, Immunity, Depression, and Disease: A Brief Overview

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Abstract: Throughout history, the term stress has come to signify modern reality. These findings will be used to examine the link between stress and sickness, focusing on the most common diseases in the Western culture like cancer and heart disease. Pathophysiological mechanisms underlying stress-induced immune alterations were researched. Studies have revealed that persistent stress is connected with the development of serious anxiety, and also a worse prognostic for heart problems, as per data. Some related studies show that stress management techniques might help people live longer. Chronic stress tends to decrease the immunological response, but acute stress has been linked to both immune activation and repression. Inflammatory cytokines, which are soluble mediators of the immune response, may cause depressive symptoms. To better understand the impact of stress in illness onset, course, and prognosis, more prospective epidemiologically based research is required. Patients with heart disease, cancer, and maybe other chronic conditions may benefit from stress management approaches that attempt to lengthen their lives. One theory is that stress and sickness are linked via alterations in the immune system. The link between depressive symptoms and stressful life events may be explained at the biological level, researchers suggest the "stress, cytokine, depression" paradigm. Future research will need to collect direct evidence for cytokine causation utilizing cytokine antagonists, like soluble Tumor Necrosis Factor (TNF) receptors, that have just recently become accessible.

Keywords: Cardiovascular Disease, Chronic Stress, Depression, Disease, Immunity, Stress.

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Introduction

The word "stress" has come to be associated with contemporary living. There are numerous widely held ideas regarding stress's negative consequences, but what proof exists that links stress to disease? Stress and sickness will be examined in this research, with anxiety, heart disease, and cancer being the three most common causes of mortality and disability in the West. The phrases "stress," "disease," and "immune system" were used in a Medline search from 1996 to 2000 to locate new studies in this subject. All relevant references discovered in all recognized publications were followed up on as well. Stress has an impact on the immune system, and modification of the immunological response may change a person's disease condition. To conclude, a model of depression pathogenesis that incorporates stress, cytokines, and depression has been developed [1].

When a person's capacity to meet environmental needs exceeds the demands of the environment, stress occurs. There are many different types of stress. It may be analyzed in terms of length, quantity, and quality. Physiological and behavioral changes accompany the perception of stimuli and response to them. There are two major parts of the stress response in terms of physiology: the hypothalamo-pituitary-adrenal axis as well as the norepinephrine/autonomic nervous systems.

Blood glucose, heartbeat, and blood pressure increase as a result of CRH activation of the parathyroid axis and the nervous system. The immunological response is regulated in tandem with behavioral changes such as increased alertness and vigilance, as well as the inhibition of eating and reproductive behavior. If the reaction is acute or short-lived, it is positive and has no negative implications [2].

Stress has been the subject of several research that have looked at its influence on the leading sources of fatality and sickness in the World today, notably cardiovascular disease, malignancy, and diabetes. Risks for these diseases are being sought for, as well as potential strategies for changing those risk factors, is, therefore, a major public health problem. Furthermore, stress has been associated with the worsening of immune-related disorders such as asthma, rheumatoid arthritis, and multiple sclerosis [3].

1.1 Coronary Heart Disease:

Concerns about stress's link to coronary heart disease have sparked research. One of the greatest well published studies was undertaken by researchers who identified personality qualities associated with "Type A" personalities, such as intense competitiveness, aggressiveness, impatience, anger, and a sense of urgency. These personality attributes would seem to produce severe stress for such "type A" character. Cardiovascular disease was examined in 3,524 Californian men aged 39 – 59 year in a retrospective epidemiological study.

Aside from a family history of coronary heart disease, smoking, high blood pressure, as well as a cholesterol level within range of “normal”, type A behavior pattern was shown to be highly associated with CHD incidence at an 8-and-a-half-year follow-up. Newer studies looked at the possibility that "Type A" people’s choices increased prevalence of cardiovascular disease might be explained by particular life circumstances. Although cancer mortality throughout this group rose unexpectedly, these researchers were unable to detect such a relationship with cardiovascular disease [4].

There was also an investigation into whether specific life events may predict cardiovascular risk. People who experienced three or even more live activities in the preceding year had a much greater mortality risk than those who hadn't, according to a survey of 752 Swedish males ages 50 and older from all causes after seven years. A protective factor seems to be enough emotional support. The number of fatalities, however, was insufficient to investigate particular reasons for death. CHD pathogenic processes are likely to have proceeded over a long period.

As a result, it's rather unsurprising that an acute stressor like a life catastrophe has little effect on the outcome a year later. Greater persistent stresses may have a role in this. Patients hospitalized for an acute ischemic event had a higher 3-year risk of re-infarction when exposed to acute and chronic stressors, with stress factors and goal disappointments having the greatest impact. A prolonged stress reaction might also cause depression indicated by hypothalamic-pituitary-adrenal (HPA)

axis activation in certain individuals, is linked to a considerably increased risk of cardiovascular morbidity and death [5]. Stress-reduction measures may be beneficial to people with coronary heart disease. Randomly assigned to undergo either standard therapy, managing stress, or exercise training were a group of 107 individuals with coronary atherosclerosis.

1.2Cancer and Stress:

A probable relationship between stress and cancer has been investigated using similar research methodologies. Breast cancer has been the subject of a lot of this research. A new meta-analysis looked at whether stressful life experiences are linked to an increased risk of cancer. The criteria for inclusion were satisfied by 29 research. There have been 14 research papers, a large prospective research and fourteen restricted controlled trials were conducted wherein women who'd been expecting the results of breast examinations were interrogated before the findings were revealed.

Women who have been told of their prognosis are more prone to exaggerate greater degrees of stress as a consequence of their illness, and this study seeks to address for memory prejudice in case-control studies by examining how women respond to their diagnosis after being notified of their diagnosis. Researchers found no connection between the risk of breast cancer and either sadness or adverse life experiences. The bulk of these studies ask about occurrences in the last two, five, or ten years, but the causative factors for breast cancer may act for many years, maybe 20 or more, prior symptoms or medical diagnostics occur. The lack of relationship between stress and breast cancer development may be due to this. It's possible that stress might have an effect on the prognosis of the condition [6].

A lot of studies have shown that reducing psychological stress improves cancer survival rates. Researchers used weekly group therapy to treat people with metastatic breast cancer. The goal of the intervention was to encourage people to talk about how to manage cancer and to convey their thoughts about the disease and its physical effects. Increased social support was given by developing relationships among group members. One year of psychosocial therapy was compared to a control group in a randomized trial. Both groups got standard cancer treatment. After 10 years of follow-up, participants in the control group had a survival rates of 36.6 months compared to 18.9 months for the control group. Patients with malignant melanoma were treated using a similar group therapy technique. Students received health education, managing stress through relaxation techniques and emotional counseling in a six-week program. When symptoms do occur, those in the intervention collective had less psychological distress after six months [7].

Stress may alter a person's immune system in a way that impacts cancer survival. There are a variety of lymphoid cells known as natural killer (NK) cells, which have the ability to lyse a broad variety of tumor and healthy cells. Viruses, bacteria, and other microbes may also be fought off with the help of these proteins. This means that cancer-fighting abilities are tied to NK cell activity, which in turn is linked to the overall health of an individual.

Study participants who had received psychotherapy for their malignant melanoma showed an increase in both the proportion and activity of their NK cells six months after the first treatment was completed. Malignant melanoma relapse was shown to be linked to baseline NK cellular activity in this cohort. Even while NK cell numbers fluctuated, neither the course of illness nor increased NK activity were shown to be associated with survival [8].

Researchers examined the impact of stress upon NK cell activity among 116 women who had had surgery for aggressive breast cancer. A questionnaire regarding intrusive and untrusting thoughts and behaviors connected to cancer was administered to patients prior to surgery in order to assess their level of stress. A decrease in spontaneous NK cell cytotoxicity was shown to be related to an increase in stress score. Furthermore, increased stress was associated with lower NK cell cytotoxicity following interferon-gamma activation (IFN-gamma).

These people's NK cells seem to have less cytotoxic potential as a consequence. Finally, Andersen observed that stress was associated with a decrease in T-cell responses, as measured by the multiplication of peripheral blood mononuclear cells in reaction to plant lectins [9]. Finally, there is substantial evidence that the outcomes of cardi-

ovascular disease, prostate cancer, and melanoma are associated to psychological stress, despite the little data presently available. Stress levels influence immune parameters, particularly NK cell cytotoxicity.

1.3Immune System and Stress:

The mechanisms by which mental trauma may have an impact on sickness outcomes are currently unclear. Several studies have looked at the influence of stressful experiences, both acute and persistent, on otherwise healthy persons who are otherwise healthy. As discussed further below, such stressors have an influence on a plethora of immunological indicators that play important role in the prevention and treatment of infection and illness.

Enumerative and functional immunological assays were used in the following research. Enumerative assays count the number of different cells of the immune system within peripheral blood or even the proportion of each kind of white blood cell. This is crucial because a precise quantity of every kind of inflammatory cells is needed to respond effectively to a viral challenge, making these tests essential. In addition to enumerative approaches, immunoglobulin (Ig) levels within saliva or extracellular fluid may be determined using immunoassays. It is possible to examine serum antibody (Ab) layers to common viral diseases, like herpes simplex virus as well as Epstein-Barr virus, because the large number of persons have been subjected to these viruses [10].

The proliferation of lymphocytes and the cytotoxic activities of natural killer (NK) cells, both of which were briefly discussed above, may be utilized to assess the functional capacity of human immune system cells. Treatment of lymphocytes in vitro using substances (mitogens) that stimulate T or B cells to divide non-specifically results in lymphocyte proliferation. The more neurons that multiply, the more effectively they act, according to conventional wisdom. Cytotoxic activity tests for NK cells measure how well they destroy damaged or changed cells (such as infected or malignant cells). To accomplish this measurement, immune cells are cultured in vitro with tumor cells [11].

1.4Life's Stressful Events:

The persons exposed to the stressful life experience of mourning had their immune system function tested by lymphocyte proliferative responses. Initial research found that these people had lower reactions, as one would expect. Researchers performed research to establish a connection between stress as well as the immune response in individuals. Despite the fact that their T and B cell counts remained unchanged, 26 bereaved couples showed a weaker lymphocyte proliferation response than a comparison group six weeks following the loss of a loved one. This research did not include a control group.

An intermediate response was obtained 4 to 14 months following bereavement. Again, no variations in total lymphocyte, T, or B cell counts were discovered. The lymphocyte proliferation response to mitogen was higher in the widows than those in the comparison group three and seven months after mourning, according to new study comparing 18 widowed to 10 young married counterparts. There was no difference in the activity of natural killer cells in the bereaved individual's vs the controls.

This group had higher proliferative responses than the control group in this research, which is intriguing. The bereaved participants' immune responses were probably suppressed over time as compared to pre-bereavement responses. In addition, unlike the other two investigations, this one included only women. As a result, stress probably affects men's and women's immune systems differently. Indeed, one research discovered that depressive female patients had more NK activity than controls, but older male sad patients have lower NK activity.

The difference in the hormonal environment might be one reason for this. Women who take estrogen and progesterone derivatives, for example, have been shown to have increased immunological activity during stressful situations. Hormone replacement therapy may have been prescribed to some of the study's participants, who ranged in age from 50 to 65. In spite of the fact that these studies reveal significant changes in immunological indicators after grieving, larger prospective models would explain the temporal evolution of these changes as well as compensate for possible confounding factors such as sex, age, and overall health [12].

Researchers looked at the link between a variety of stressful life experiences and the immunologi-

cal response. Academic stress among medical students was first the focus of this study group's attention as a prevalent stressful scenario. The immunological responses were lowered relative to the pre-examination background during the final examination period. The number of activated lymphocytes, the activity of natural killer (NK) cells, and the production of interferon by these cells all reduced. Detection of increased antibody levels to latent herpesviruses, that might indicate decreased immune cell function, was also found. Research has shown that the immunological response's outcome may be affected by the subject's perception of stressors and social support, among other things. Adolescents who experienced stronger social support in the first place of the third vaccination exhibited higher antibody titers against hepatitis B membrane antigen just at time of an immunization.

Rather from suppressing the immunological response, research has demonstrated that acute stress stimulates it in certain cases. a day or two before a test, the immune system is more active as shown by an increase in neutrophils, monocytes. Stress was measured using the Perceived Stress Scale, and the findings were compared to baseline and post-exam answers. Students who did not exhibit a rise in stress levels (stress non-responders) did not demonstrate substantial alterations in their immune systems.

Activated T and B lymphocytes, as well as increased lymphocyte proliferation or NK cell cytotoxicity, have all been linked to immune activation during testing. This study's participants learned self-hypnosis as a way to cope with stress. These participants reported considerably less discomfort and anxiety than their non-intervention peers, but there was no difference in immunological function between the two groups. Those patients reporting greater degrees of relaxation in the self-hypnosis group, on the other hand, demonstrated increased NK cell cytotoxicity during the study [13].

These related studies show that when medical students are under test stress, their immune system function changes. There has been evidence of both immune suppression and stimulation. Individuals' psychological responses to test stress seem to affect whether or not changes occur. There is no apparent reason why some research shows increased immune activity under test stress while others show suppression. Individuals in certain research were probably exposed to chronic stress, leading to a change in the immunological response.

1.5Enduring Stressors:

Care givers of Alzheimer's illness, children with disabilities, and mothers of babies with an exceptionally low birth weight have all been examined. As a result, many investigations are biased towards female individuals by their very nature. Several components of the immune response are downregulated in these investigations. Caregiving for Alzheimer's patients has been linked to changes in lymphocyte subpopulations, increased herpes simplex virus antibody titers, decreased proliferative responses to mitogens, more days of infectious disease illness than matched controls, impaired antibody responses to an influenza virus vaccine, and a longer latency in wound healing.

Patients with Alzheimer's disease and their caretakers were compared on the basis of immunological features to 18 other people of similar age and sexual orientation. T-cells in caregivers were lower, T suppressor cells were higher, and the T helper ratio was lower than in the general population. There was a significant difference in the number of T cells as well as T helper cells between the 2 groups whenever the median age of both the patients was taken into account. Immune system function may be impacted by these alterations in immunological characteristics. Cytokines produced by T helper cells, T cytotoxic cells, especially T suppressor cells boost the immune system, while T helper cells themselves lyse cells attached to them. It's also worth noting that, as previously said, elevated viral antibody titers have been linked to reduced cellular immunity in various stressful contexts [14].

In a second practical example of chronic stress, researchers identified the experiences of mothers of prematurely born, extremely premature babies. As caretakers, these females could be particularly sensitive to strain immunologic enzyme inhibition, despite the fact that they are still reestablishing resistance to infection after the physiological alterations that occur during prenatal development. In a research conducted in the United States, 25 mothers had preterm VLBW infants who survived and were sent home, while 25 mothers had preterm infants of average weight. When compared to moms of term babies, moms of pre-term

VLBW babies showed reduced mitogen response throughout the first three months after delivery.

There were almost no distinctions in terms of health habits such as food, smoking, or physical activity. Anxiety and despair were unable to explain the association, therefore the scientists hypothesized that the continuous stressor of caring for a tiny, delicate newborn was to blame. The activity of NK cells in the two groups of moms was identical. This shows that stress has different effects on different parts of the immune system. Furthermore, specific immunological components may be impaired after some time [15], [16,17-21].

2. Discussion

The findings of this study show that alterations in the immune system occur as a result of stress. These studies, however, show physiological heterogeneity in the immune stress response, but they don't tell us anything about the clinical consequences of such alterations. Stress-induced alterations in immune response have the potential to reduce host resistance to pathogenic pathogens. Several research, including the ones described above, have revealed that caregivers of Alzheimer's disease patients have an increased number of days of sickness due to infectious infections. However, a series of "experimental research" yielded additional information on the subject. Psychological stress was shown to increase the likelihood of URTIs and worsen the symptoms associated with them, according to these studies.

Stress levels were monitored during the virus was made available to the participants. This study found a dose-response relationship between higher stress and an elevation in infection risk. Acute stress is not connected to the development of colds, however severe chronic stress (lasting one month or more) has been linked to a significantly higher risk of illness. These results are consistent with the previous experimental data linking chronic stress (e.g., caregiving) to immune response reduction.

Clinically significant immunological modifications have been bolstered with this research since it provides a possible reason for the relationship between stress as well as intensity of symptoms, elevated interleukin 6 production (IL-6). IL-6 is produced both in vitro as well as in vivo when rhinoviruses are introduced to epithelial cells. Researchers found a relationship between illness severity and variations in IL-6 output. Flu A virus was experimentally afflicted with 55 adult volunteers following a psychological stress test. Quarantined patients had their upper respiratory discomfort, mucus production, including IL-6 levels via nasal lavage monitored on a regular basis. In all three tests, the greater the amount of psychological stress, the better the outcomes. Experimental cytokine injections in animals and humans have been linked to influenza-like symptoms.

Stress has been shown to raise IL-6 levels in mammals in a number of studies. Humans have also been shown to produce cytokines as a reaction to stress. Medical students that were under test pressure had higher levels of pro-inflammatory cytokines including IL-1b and TNF-a in their blood. In another study, an artificial stressor induced higher levels of IL1b and TNF-a in patients with rheumatoid arthritis and healthy controls. An artificial laparoscopic incision is associated with reduced concentrations of IL-1 inside the direct proximity of chronic stress.

Chronic stress has indeed been found to have an effect on the immune system. As we'll see in a moment, one of the molecular mechanisms through which stress results in depression is an increase in the synthesis of pro-inflammatory cytokines during activated due to the sudden. Depression and recurrence were linked to psychological stress. Before a depressive episode begins, there are usually many stressful life events that occur, according to the research. This community-based study in Camberwell, South London, found susceptibility variables that raise the likelihood of depression in the presence of a provoking agent.

In a separate prospective community-based research, poor self-esteem was identified as a key susceptibility factor, and those who lacked assistance from a close relative during a crisis were shown to be at a much higher risk of recurrent depression. Chronic stress as well as a life event increase the risk of depression, therefore it appears that depression is more common in those who have both chronic and acute stressors. The biochemical processes behind such an impact, however, have yet to be discovered.

One reason for such an impact might be a "stress, cytokine, depression" paradigm. Stress, according to our theory, causes proinflammatory cytokine

release, which causes behavioral and hormonal abnormalities ("illness behavior"), which eventually leads to depressive symptoms. Proinflammatory cytokines such as interleukin-1 (IL-1) and interleukin-6 (IL-6) and tumor necrosis factor (TNF) control the acute phase reaction, which is an early immune response to invading pathogens. The goal of the acute phase response is to minimize tissue damage, isolate and eliminate the invading organism, and activate healing mechanisms.

While such immune activity may prevent harm from invading microorganisms, it may also cause unpleasant and painful symptoms. Proinflammatory cytokines have been shown to cause a set of behavioral characteristics known as "ill behavior." Extreme bacterial or viral diseases are often accompanied by symptoms such as exhaustion, anorexia, anorexia nervosa, apathy, depression, and a general feeling of malaise. High-dose cytokine treatment is used to treat cancer or viral illness, and patients show signs of illness as a side effect.

Sickness behaviour overlaps with the symptoms of various mental illnesses (especially major depression), which suggests that cytokines released under stress may have a role in behavioural anomalies in stress-related illnesses like major depression. Studies suggest that proinflammatory cytokines may trigger the secretion of corticotrophin-releasing factor (CRF) and adrenocorticotrophic hormone (ACTH), resulting in HPA axis hyperactivity comparable to that seen in severe depression. Finally, some studies have found higher levels of interleukin-1 (IL-1), tumour necrosis factor (TNF), and more consistently, interleukin-6 (IL-6) in people suffering from major depression.

3. Conclusion

It has been the topic of this review to look at the interaction between stress, illness, depression, as well as the immune system. According to current research, stress is a potential health hazard for cardiovascular disorders. Wonderful forum studies are needed to resolve this debate, and more culture studies are being planned. According to the research undertaken, stress would seem to be connected with a worse prognosis in both conditions, and the limited studies that have been completed show that review was written therapies are associated with increased survival in both situations. The development and relapse of severe depression are linked to stressful life events and conditions.

Many immunological markers tested under acute and chronic stressful circumstances show changes. It's unclear what clinical relevance such modifications have. Changing levels of an immunological measure (IL-6) have been shown to be associated with deteriorating clinical manifestations of a higher respiratory infection, according to one study. Aside from just managing the immune response, a few of these alterations in immunological variables, such as increased proinflammatory cytokines, could have an influence on mood and behaviour as well as on the immune reaction itself. It is true that proinflammatory cytokines like interleukin 1, interleukin 6, and tumour necrosis factor (TNF) have the ability to induce "sickness behaviour," which is a characteristic of depression, leading to the theory that cytokines might play a pivotal role in the pathogenesis of depression.

This concept is now being investigated by our group using several methods. To begin, we looked at the molecular processes through which proinflammatory cytokines might cause depression. According to study, the inflammation cytokine obtain the level may cause HPA axis aberrations that are analogous to those observed in depressed people by affecting the molecular processes by which it does so. Note that the molecular alterations generated by proinflammatory mediators seem to be fundamentally opposed toward those produced by pharmaceuticals in the vast majority of instances.

Secondly, we looked at the relationship between a person's previous or recent mental history as well as the psychopathological symptoms caused by interferon-alpha treatments for patient's viral hepatitis. Interferon-alpha stimulates the synthesis of proinflammatory cytokines, which are released into the body. Researchers examined symptoms of sorrow, tiredness, and general well-being in this group of patients. A fascinating theoretical underpinnings in which to start investigating and generate more suppositions about the biochemical pathways of depression pathogenesis, scientists claim, is that stressful life interactions may precede the development of anxiety by causing the expression of inflammatory cytokines as a result of their effects on the release of cytokines.

In the future, it will be essential to acquire direct evidence for the causal function of cytokines, which will be accomplished via the use of cytokine antagonists, like soluble TNF receptors, that have just recently been commercially accessible. Through the utilization of such substances, it is possible to better understand the role played by particular cytokines mostly in the psychological consequences of endotoxin. Finally, different experimental paradigms of immune activation, as well as cytokine release, should be employed to establish the long-term consequences of the drug.

References:

[1] C. Maddock and C. M. Pariante, "How does stress affect you? An overview of stress, immunity, depression, and disease," Epidemiologia e Psichiatria Sociale. 2001, doi: 10.1017/S1121189X00005285.

[2] F. Novellino et al., "Innate immunity: A common denominator between neurodegenerative and neuropsychiatric diseases," International Journal of Molecular Sciences. 2020, doi: 10.3390/ijms21031115.

[3] S. Zhu et al., "The progress of gut microbiome research related to brain disorders," Journal of Neuroinflammation. 2020, doi: 10.1186/s12974-020-1705-z.

[4] L. J. Kang et al., "Maternal psychological distress before birth influences gut immunity in mid-infancy," Clin. Exp. Allergy, 2020, doi: 10.1111/cea.13551.

[5] B. Szmyd et al., "Attitude and behaviors towards sars-cov-2 vaccination among healthcareworkers: A cross-sectional study from Poland," Vaccines, 2021, doi: 10.3390/vaccines9030218.

[6] G. Casey, "Stress and disease," Kai Tiaki Nurs. New Zeal., 2017, doi: 10.1093/ptj/49.3.320b.

[7] E. Effendy, M. M. Amin, L. de Vega, and N. Utami, "The association between CD-4 level, stress and depression symptoms among people living with HIV/AIDS," Open Access Maced. J. Med. Sci., 2019, doi: 10.3889/oamjms.2019.446.

[8] S. Masafi et al., "Effect of stress, depression and type d personality on immune system in the incidence of coronary artery disease," Open Access Maced. J. Med. Sci., 2018, doi: 10.3889/oamjms.2018.217.

[9] M. R. Irwin, "Human psychoneuroimmunology: 20 Years of discovery," Brain. Behav. Immun., 2008, doi: 10.1016/j.bbi.2007.07.013.

[10] Z. Adam, Z. Král, J. Klimeš, Z. Boleloucký, and L. Pour, "Chronic stress, mental discomfort, and depression increase the rates of infectious, autoimmune as well as malignant diseases," Vnitr. Lek., 2020, doi: 10.36290/vnl.2020.006.

[11] C. G. Engeland et al., "Psychological distress and salivary secretory immunity," Brain. Behav. Immun., 2016, doi: 10.1016/j.bbi.2015.08.017.

[12] S. Cohen and T. B. Herbert, "Health Psychology: Psychological Factors and Physical Disease from the Perspective of Human Psychoneuroimmunology," Annu. Rev. Psychol., 1996, doi: 10.1146/annurev.psych.47.1.113.

[13] Y. B. Lee, E. J. Byun, and H. S. Kim, "Potential role of the microbiome in acne: A comprehensive review," Journal of Clinical Medicine. 2019, doi: 10.3390/jcm8070987.

[14] R. K. Dishman et al., "Neurobiology of exercise," Obesity, 2006, doi: 10.1038/oby.2006.46.

[15] M. Reich, A. Lesur, and C. Perdrizet-Chevallier, "Depression, quality of life and breast cancer: A review of the literature," Breast Cancer Research and Treatment. 2008, doi: 10.1007/s10549-007-9706-5.