

The Islamic Perspective of Spiritual Intervention Effectiveness on Bio-Psychological Health Displayed by Gene Expression in Breast Cancer Patients

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Received 2016 April 12; Accepted 2016 April 17.

Abstract

Background: During the last two decades, there have been spiritual/religious interventions in cancer patients to prevent or treat a range of physical problems, including managing chronic pain, coping with the disease, boosting hope and mental health. Although societies are of different faiths and belief systems, what they all share is spirituality.

Objectives: Upon this we put forward the hypothesis of changes in gene receptor expressions as a result of spiritual intervention for the first time in the world.

Materials and Methods: In this study, the spiritual intervention was conducted on 57 volunteer females with early breast cancer involvement. Blood samples were collected prior to and after the spiritual intervention to analyze the changes in dopamine gene receptor expressions as the main site of effect. In order to administer the spiritual intervention backed by Quran, Islam and international standards, issues, with emphasis on peace, human growth and perfection, accepting God as an eternal source of power and kindness to build trust and reduce stress, were selected. They included prayer, patience, reliance, self-sacrifice and forgiveness, altruism and kindness, remission and repentance, thankfulness, zikr (mantra), meditation, and death concept.

Results: Obtained results from peripheral blood mononuclear cell samples analyzed by real time-PCR showed significant reduction in dopamine gene receptor (DRD1-5) expressions in comparison with those of pre-test scores and the control group.

Conclusions: Spiritual intervention based on Islamic principals can bring back mental health, increase hope and quality of life and eventually change dopamine gene receptor expressions resulting in reduction of cell proliferation, thus better prevention and management in breast cancer patients compared to other forms of treatment.

Keywords: Spiritual Intervention, Islamic Perspective, Gene Expression, Breast Cancer

1. Background

Human and only human is an absolute creature with all materialistic and spiritual features. In His holy verses (Alhijr, 10) (1) God recognizes human beyond the mere physicality by fashioning him from soil and then breathing His spirit into him. He puts upon his shoulder nothing but to serve Him (Zaryiat, 56) (1) which in fact is a responsibility on man's spirituality through his physicality. Human's spiritual and physical dimensions are interwoven in his creation and inseparable till death takes them apart. Motahari (2) refers to this as spirituality and physicality inter-affecting one another. During the last two decades, there have been spiritual/religious interventions in cancer patients to prevent or treat a range of physical problems, including managing chronic pain, coping with the disease, boosting hope, increasing quality of life and mental health. Koenig (2012) showed, in his review, a funda-

mental change in studies related to spirituality and religion from 1971 to 2012 (e.g. from 2002 to 2012, the number of studies investigating various effects of spirituality on physical and mental dimensions was 7-fold those of the last 30 years) (3). Spirituality is a universal keyword and representative of search for meaning, perfection and salvation (4). Although societies are of different faiths and belief systems, what they all share is spirituality (5). Of these, some do not differentiate between religion and spirituality, some differentiate the two, some recognize spirituality as part of religion and some others lean toward religion as the basis (6-12). Spirituality is often known in relation with their inner motivations and their emotional relationship with their god(s) (13). While other societies have not yet reached a consensus on the common definition of spirituality (14), Islamic sources have a clear definition for spirituality. To put it in Motahari's terminology, spirituality in view of Quran is the basis for perfec-

tion, and it is mostly faith in God and right deeds and behavior or in other words: serving God. In the main study, which is the first one of its kind in the world, conducted by the authors on these very principles, we managed to revive spiritual behaviors in a group of cancer patients leading to changes (the cell biological changes begin with changes in its genes) in their gene receptor expressions so much that genetic stress factors were controlled and the patients were able to experience significantly calmer and more peaceful (15). This is due to the fact that, based on a literature review, with chronic stress, dopamine concentration increases leading to an inhibitory effect on T-cells which in turn expands cancer (16).

2. Objectives

The present study is also an attempt to show the effects of spiritual intervention on gene receptor expressions and behavior modifications in patients based on Islamic principles. The decision stems from causality rules as the main religious guideline of the authors. This is clearly reflected in a Hadith by Imam Sadeqh, Peace be upon him “God refrains from running affairs but by their causes. Thus He has appointed a cause for any effect, an expression for any cause, knowledge for any expression and a way for acquiring any knowledge.” Upon this, we put forward the hypothesis of changes in gene receptor expressions as a last terminal biological result of spiritual intervention.

3. Materials and Methods

3.1. Participants

58 women suffering from primary breast cancer took part in this study based on inclusion and exclusion criteria and were placed in two groups: experimental and control, with 28 and 29 people respectively. Blood samples were collected prior to and after the intervention to analyze the changes in dopamine gene receptor expressions.

3.2. Concepts

In order to administer the spiritual intervention backed by Quran, Islam and international standards, issues, with emphasis on peace, human growth and perfection, accepting God as an eternal source of power and kindness to build trust and reduce stress, were selected. They included prayer, patience, reliance, self-sacrifice and forgiveness, altruism and kindness, remission and repentance, thankfulness, mantra, meditation, and death concept.

3.3. Structure

The mentioned spiritual issues were presented in 10 weekly sessions of 90 minutes each. The framework of a given session is presented in the following Table 1.

Table 1. Framework of a Given Session

Session	Spiritual Issue
1.	Prayer in the beginning, in order to establish a spiritual presence and to feel closer to God.
2.	Relaxation
3.	Review of material from the previous session as well as the homework
4.	Explanation of the topic at hand for the session with participation of members
5.	Discussion of the topic at hand by members using spiritual/religious and Islamic issues
6.	Summarizing and conclusion
7.	Homework
8.	Ending the session by prayer
9.	Personal consultation
10.	Transcribing discussed topics

3.4. Procedure

Thus blood samples were obtained from healthy people as controls. Blood samples were obtained from breast cancer patients prior to and after the spiritual intervention as the case group by means of real-time PCR in order to assess the dopamine gene receptor expressions. Participants attended the study with a background of belief in Islam, thus Islamic issues can be explained separately in sessions.

3.5. Prayer

Prayer is an expression of indigence before God when one is desperate of other sources. In other words, “Those who believe, and whose hearts find satisfaction in the remembrance of Allah: for without doubt in the remembrance of Allah do hearts find satisfaction” (Rad, 28) (1). Another verse emphasizes the necessity, “Say [to the Rejecters]: “y Lord is not uneasy because of you if ye call not on Him”, God says, “Call on Me; I will answer your [Prayer]” (Ghafir, 60) It should be noted that prayer cannot replace efforts and hard work, but rather it completes them. Imam Ali says, He who prays and does nothing else is shooting an arrow without the bowstring” (17). Therefore, we did not replace any of conventional treatments with spiritual factors, but we used it as a useful complementary treatment.

3.6. Patience

“seek help with patient perseverance and prayer” (Baqarah, 153) (1). Although God clearly states, “verily We have created man into toil and struggle” (Balad, 4) (1), yet He advises man to patience repeatedly (e.g. Bagharah, 131 (1)) and adds, “O ye my servants who believe! Fear your Lord, good is [the reward] for those who do good in this world. Spacious is Allah’s earth! Those who patiently persevere will truly receive a reward without measure!” (Zumar, 10) (1).

3.7. Reliance

It is relying on someone else for your affairs; admitting weakness and ignorance, one relies on a qualified, trustworthy source of wisdom (18). Quran reassures people that the relation between reliance and faith is undeniable and guarantees its effectiveness (Maida, 11 and 23; All-i-Imran, 122 and 160; Anfal, 49; Abraham, 11; Tauba, 51; Mujadilah, 10) (1). Imam Ali says that faith has four pillars: reliance on Allah, assigning affair to Allah, satisfaction with His will and obedience to His orders (19). Allah says, “And if any one puts his trust in Allah, sufficient is [Allah] for him.” (Talagh, 3) (1).

3.8. Alms

People give alms to purify and sanctify themselves (Tauba, 103) (1). Those who give in charity will have their rewards with Lord (Bagharah, 274) (1), will please Him, be free of fears and be bestowed by His blessings (Al-i-Imran, 180) (1). “The parable of those who spend their substance in the way of Allah is that of a grain of corn: it groweth seven ears, and each ear hath a hundred grains. Allah giveth manifold increase to whom He pleaseth: And Allah careth for all and He knoweth all things” (Bagharah, 261) (1). “Those who spend [freely], whether in prosperity, or in adversity; who restrain anger, and pardon [all] men; for Allah loves those who do good” (All-i-Imran, 134) (1).

3.9. Altruism and Kindness

Loving others is a key concept in holy Quran. The first verse of Quran, “In the name of Allah, Most Gracious, Most Merciful”, is a manifestation of mercy and love. Faith and love are inseparable. God says that those who have faith, love God more. As human goes further on the path of faith, he falls deeper in love with his goal and finds more pleasure (20). “On those who believe and work deeds of righteousness, will [Allah] Most Gracious bestow love” (Maryam, 96) (1). That is to say kindness generates kindness as God says to the holy prophet Muhammad, “It is part of the Mercy of Allah that thou dost deal gently with them

Wert thou severe or harsh-hearted, they would have broken away from about thee: so pass over [Their faults], and ask for [Allah’s] forgiveness for them; and consult them in affairs [of moment]” (Al-i-Imran, 159) (1).

3.10. Repentance

Repentance is a meaningful relationship that keeps people closer to God, those who were on the path to part from Him. Repentance is the most effective measure to seek spirituality that is knowing God and right deeds. God speaks of these in various verses (Al-i-Imran, 135; Nissa, 110; Hood, 11; Tauba, 27; Shuaraa, 13 and 25; Anam, 54) (1). The key point here is that repentance is not accepted in defiance and rejecting (Al-i-Imran, 90 and 92) (1). Thus this component brings about prerequisites one needs to reform oneself and get closer to God.

3.11. Thankfulness

Thankfulness means using God’s blessings in the way they were aimed at their creation. Thankfulness is key to grace and value of self, and attracts people onto God. God Himself is thankful and appreciated those who give (Tagabun, 17) (1) and He says, “If ye are grateful, I will add more [favours] unto you” (Abraham, 7) (1); “Any who is [so] grateful does so to the profit of his own soul” (Luqman, 12; Bagharah, 56) (1).

3.12. Mantra

Mantra (zikr) is the remembrance God in a devotional act and admitting His presence to meet human needs, and with it comes satisfaction and peace, “for without doubt in the remembrance of Allah do hearts find satisfaction” (Rad, 28) (1).

God says, “O ye who believe! Celebrate the praises of Allah, and do this often” (Ahzab, 41) (1) and says, “But whosoever turns away from My Message, verily for him is a life narrowed down” (Ta Ha, 124) (1). “The most beautiful names belong to Allah: so call on him by them; but shun men as use profanity in his names: for what they do, they will soon be requited” (Araf, 180) (1).

3.13. Meditation

It is the most effective way in reforming one’s behavior and persistence of right deeds. (Maida, 105) (1). Prophet Muhammad did emphasize on weighing one’s deeds. Meditation causes rectifying mistakes and timely correction of deeds and behaviors.

3.14. Death Concept

Death, the most certain incidence in life, is the most complicated concept. But Islam and psychology agree that emotional reactions of people to death and accepting death highly depend on their deeds, behaviors, thoughts, personality, and coping capabilities. God created death and puts it ahead of life (Mulk, 2) (1); He does not know death as the end of life but rather a new beginning (Zumar, 42; Waqia, 60; Anbyia, 34) (1). God brings the dead to life and this is one of His signs (Yunus, 56; Bagharah, 73) (1). Imam Sajad peace be upon him says, “death to believers is like ridding themselves of filthy and ragged clothes filled with bugs, and breaking free of heavy chains and shackles; instead change into scented elegant clothes, tamed horse and glorious houses. Or it feels like sleep only much longer (21).

Bearing in mind the religious/Islamic factors mentioned above, we designed a 10-session intervention of 120 minutes each session with “to do at home exercises” in order to revive and re-establish the spiritual concepts within individuals. Every session would begin with prayer and then information on definition, cognition, and experience of the mentioned concepts were elicited in form of questions. The therapist(s) would then continue with follow-up questions to later establish the concepts upon the responses. Homework was assigned to participants based on the established concepts which were reviewed in the following session to address possible questions. Then blood samples were collected from the healthy individuals as control group, and from cancer patients as the case group both prior to and after the intervention. Gene expressions were measured and studied by real-time PCR.

4. Results

Obtained results, as thoroughly explained in our previous study (15), from peripheral blood mononuclear cell samples analyzed by Real time-PCR collected from patients who underwent the conventional treatment together with the spiritual intervention showed significant reduction in dopamine gene receptor expressions in comparison with those of pre-test scores and the control group (Tables 2 and 3).

5. Discussion

Cancer is known as the major health threat of the century given rise to by inadequate nutrition, rising life span average, lack of physical activities, smoking, drinking alcohol, and chronic stress (22). Interventions to control causes of cancer are typically educational based programs to raise

Table 2. Experimental Group Peripheral Blood Monocle (PBMC) Pre-Test Scores Compared to Post-Test Scores

Dopamine Receptors	Rate of Change	Standard Error	P Value ^a
DRD1	9.81	± 1.70	0.001***
DRD2	8.11	± 0.89	0.001***
DRD3	8.56	± 0.97	0.001***
DRD4	6.94	± 0.73	0.001***
DRD5	2.56	± 0.63	0.004**

^a*** Significant decreasing at $P \leq 0.001$ level (down regulation), ** Significant decreasing at $P \leq 0.01$ level (down regulation), and * Significant decreasing at $P \leq 0.05$ level (down regulation).

Table 3. Experimental Group PBMC Compared to PBMC in Control Group

Dopamine Receptors	Rate of Change	Standard Error	P Value ^a
DRD1	8.61	± 0.84	0.001***
DRD2	10.73	± 0.77	0.001***
DRD3	11.8	± 1.0	0.001***
DRD4	8.90	± 0.7	0.001***
DRD5	3.7	± 0.73	0.004**

^aSee footnote of Table 2.

awareness resulting in changes in patients’ behavior. However, to come to terms with stress factors and to control chronic stress, there are various solutions, mostly psychological ones. Many are the studies reporting the positive effects of psychological interventions in reducing stress, depression and better coping with physical-psychological damages (23, 24). Spiritual interventions have been shown to generate positive effects in fighting against physical problems caused by cancer including chronic pain, fear of death, hope and mental health (25-28). Chronic stress manipulates the immune system through changes in catecholamine and cortisol release and eventually results in a reduction in protective cells especially T-cells activities (29). It also brings about lower quality of life, disruption in mental health, reduction of hope, and increase in anxiety and depression (30, 31). Spiritual interventions have been able to generate positive outcomes in all these cases (32-34) and based on previously mentioned verses, (e.g. surely in the remembrance of god do hearts find rest (Rad, 28) (1)), they could reduce chronic stress.

The authors of this study designed a spiritual intervention for the first time in the world based on the philosophy of causality and based on a Hadith from Imam Sadigh, “Allah doth everything in its natural way by means of known causes” (21), to discover the changes in dopamine gene receptor expressions as the final result of biological

effect of spirituality. These manipulations generated direct effects in reducing chronic stress as well as cell proliferation (35, 36). There are important neurotransmitter pathways in the neuroendocrine system that control secretion of other neurotransmitters, like dopamine, serotonin, glutamate, etc. And they can play roles in causing or treating diseases via their interaction with other systems (37). Dopamine receptors and transmitters functioning in nerves have the capability to indirectly predict diseases or even worse directly cause diseases (37). In a study by Terasaka et al. conducted in 2000, they showed the reducing effects of dopamine (dose dependent) on the number of living cells in salivary gland tumors and squamous cell carcinoma (38). Also, Gutzkow et al. in a similar study back in 2003 showed that dopamine affects cAMP proliferation in T-cells and hinders their proliferation. Since the link between dopamine and its receptor increases cAMP proliferation, this secondary messenger has a regulatory function in cell proliferation and hinders lymphocyte proliferation (39). Hence a substantial increase in inhibitor receptors can weaken the immune system and in turn affects proliferation and induces spread of the disease. Dopamine is the stress related hormone. cancer patients experience stress from two sources: the chronic stress because of 3 to 5 years prior to cancer, and stress because of cancer and possibility to lose their job, to be socially isolated, to have financial problems, to spend a lot of time in chemotherapy or radiation therapy and the expenses. Therefore, due to the fact that stressful events can weaken the immune system and transform the disease from primary stages of neoplasm growth to higher stages of cancer (40), spiritual intervention can generate peace by reducing stress. As a result, by affecting the nervous system, it can regulate and balance in immune cell receptors (15).

Evidently, if spiritual factors are practiced, they can reduce stress factors and thus cell proliferation by changes in gene receptor expressions including dopamine gene receptor expressions and the consecutive epigenetic changes. Pornour et al. studied changes in dopamine gene receptors in breast cancer patients and healthy subjects and showed that DRD1-DRD4 dopamine gene have increased significantly in cancer patients accompanied by cell proliferation (41). These studies showed that chronic stress had direct effects on dopamine and its impact on recurrence or spreading of the cancer, and that spiritual therapy had positive effects in reducing stress and changing dopamine gene receptor expressions. In this study, we considered verses from the Holy Quran and Hadiths from the holy prophet Muhammad and his successors. In fact, changes in dopamine gene receptors give rise to cell proliferation and the spiritual intervention proved to have anti-cancer effects.

5.1. Conclusion

Spiritual intervention based on Islamic principals can bring back mental health, increase hope and quality of life and eventually change dopamine gene receptor expressions resulting in reduction of cell proliferation, thus better prevention and treatment in breast cancer patients compared to other forms of treatment.

Acknowledgments

Special thanks for breast cancer patients and other colleague of cancer research center.

Footnotes

Authors' Contribution: Study concept and design: Mohammad Esmaeil Akbari; acquisition of data: Leili Hosseini; analysis and interpretation of data: Saeedeh Sarafrazmehr; drafting of the manuscript: Saeedeh Sarafrazmehr; critical revision of the manuscript for important intellectual content: Farah Lotfi Kashani; statistical analysis: Saeedeh Sarafrazmehr; administrative, technical, and material support: Leili Hosseini; study supervision: Mohammad Esmaeil Akbari.

Conflict of Interest: There was no conflict of interest to be declared.

Financial Disclosure: The authors that they have no competing interest.

Funding/Support: This study was supported in part by grant and by a teaching and research scholarship from the cancer research center.

References

1. Yusuf Ali A. The Holy Qur'an [Translated]. Amana: Brentwood, MD; 1991.
2. Motahari M. Nabowvat [in Persian]. Tehran: Sadra; 2011.
3. Koenig HG. Religion, spirituality, and health: the research and clinical implications. *ISRN Psychiatry*. 2012;2012:278730. doi: [10.5402/2012/278730](https://doi.org/10.5402/2012/278730). [PubMed: [23762764](https://pubmed.ncbi.nlm.nih.gov/23762764/)].
4. Hinnells JR. The Routledge companion to the study of Religion. New York: Psychology Press; 2005.
5. Wulff D. Psychology of Religion. In: Leeming DA, editor. *Encyclopedia of Psychology and Religion*. Boston, MA: Springer US; 2014. pp. 1424-9.
6. Murray SA, Kendall M, Boyd K, Worth A, Benton TF. Exploring the spiritual needs of people dying of lung cancer or heart failure: a prospective qualitative interview study of patients and their carers. *Palliat Med*. 2004;18(1):39-45. [PubMed: [14982206](https://pubmed.ncbi.nlm.nih.gov/14982206/)].
7. Clifford M, Gruca JA. Facilitating spiritual care in the rehabilitation setting. *Rehabil Nurs*. 1987;12(6):331-3. [PubMed: [3423419](https://pubmed.ncbi.nlm.nih.gov/3423419/)].
8. Krishnakumar S, Neck CP. The "what", "why" and "how" of spirituality in the workplace. *J Managerial Psychol*. 2002;17(3):153-64. doi: [10.1108/02683940210423060](https://doi.org/10.1108/02683940210423060).
9. Mitroff II, Denton EA. A study of spirituality in the workplace. *MIT Sloan Manage Rev*. 1999;40(4):83.

10. Marques SC, Lopez SJ, Mitchell J. The Role of Hope, Spirituality and Religious Practice in Adolescents' Life Satisfaction: Longitudinal Findings. *J Happiness Studies*. 2012;**14**(1):251-61. doi: [10.1007/s10902-012-9329-3](https://doi.org/10.1007/s10902-012-9329-3).
11. Chuengsatiansup K. Spirituality and health: an initial proposal to incorporate spiritual health in health impact assessment. *Environ Impact Asses*. 2003;**23**(1):3-15. doi: [10.1016/s0195-9255\(02\)00037-9](https://doi.org/10.1016/s0195-9255(02)00037-9).
12. Korac-Kakabadse N, Kouzmin A, Kakabadse A. Spirituality and leadership praxis. *J Managerial Psychol*. 2002;**17**(3):165-82. doi: [10.1108/02683940210423079](https://doi.org/10.1108/02683940210423079).
13. McCormick DW. Spirituality and Management. *J Managerial Psychol*. 1994;**9**(6):5-8. doi: [10.1108/02683949410070142](https://doi.org/10.1108/02683949410070142).
14. Schultz D. Growth psychology: Models of the healthy personality. New York: D. Van Nostrand; 1977.
15. Akbari ME, Kashani FL, Ahangari G, Pornour M, Hejazi H, Nooshinfar E, et al. The effects of spiritual intervention and changes in dopamine receptor gene expression in breast cancer patients. *Breast Cancer*. 2015;1-8. doi: [10.1007/s12282-015-0658-z](https://doi.org/10.1007/s12282-015-0658-z). [PubMed: [26597879](https://pubmed.ncbi.nlm.nih.gov/26597879/)].
16. Mancino M, Ametller E, Gascon P, Almendro V. The neuronal influence on tumor progression. *Biochim Biophys Acta*. 2011;**1816**(2):105-18. doi: [10.1016/j.bbcan.2011.04.005](https://doi.org/10.1016/j.bbcan.2011.04.005). [PubMed: [21616127](https://pubmed.ncbi.nlm.nih.gov/21616127/)].
17. Razi S. Nahj olbalaghe [in Persian translated by Mohammad Dashtai]. Qom, Iran: Amiralmomenin research institute; 2005.
18. Sharaf Yektaei B. Ayat-e Elahi [in Persian]. Tehran: Hoormazd; 2013.
19. Tabatabaei MH. Manavit-e Tashayyo [in Persian]. Qom, Iran: Tashayyo; 2011.
20. Janadi Amoli A. Tafsir Tasnim [in Persian]. Qom, Iran: Asra; 2014.
21. Majlesi MB. Behar-ol Anvar [in Arabic]. Tehran, Iran: Eslamieh; 2000.
22. Brinton L, Lacey J, Devesa S. Epidemiology of breast cancer. *Cancer of the Breast*. 2002;**5**:111-32.
23. Brown KW, Levy AR, Rosberger Z, Edgar L. Psychological distress and cancer survival: a follow-up 10 years after diagnosis. *Psychosom Med*. 2003;**65**(4):636-43. [PubMed: [12883115](https://pubmed.ncbi.nlm.nih.gov/12883115/)].
24. Kubzansky LD, Thurston RC. Emotional vitality and incident coronary heart disease: benefits of healthy psychological functioning. *Arch Gen Psychiatry*. 2007;**64**(12):1393-401. doi: [10.1001/archpsyc.64.12.1393](https://doi.org/10.1001/archpsyc.64.12.1393). [PubMed: [18056547](https://pubmed.ncbi.nlm.nih.gov/18056547/)].
25. Meraviglia M. Effects of spirituality in breast cancer survivors. *Oncol Nurs Forum*. 2006;**33**(1):E1-7. doi: [10.1188/06.ONF.E1-E7](https://doi.org/10.1188/06.ONF.E1-E7). [PubMed: [16470229](https://pubmed.ncbi.nlm.nih.gov/16470229/)].
26. Paloutzian RF, Park CL. Handbook of the psychology of religion and spirituality. New York: Guilford Publications; 2014.
27. Park CL, Paloutzian RF, Park CL. Religion and meaning. In: Paloutzian RF, Park CL, editors. Handbook of the psychology of religion and spirituality. New York: Guilford Publications; 2005. pp. 295-314.
28. Kappelman MD, Rifas-Shiman SL, Kleinman K, Ollendorf D, Bousvaros A, Grand RJ, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol*. 2007;**5**(12):1424-9. doi: [10.1016/j.cgh.2007.07.012](https://doi.org/10.1016/j.cgh.2007.07.012). [PubMed: [17904915](https://pubmed.ncbi.nlm.nih.gov/17904915/)].
29. Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES. The sympathetic nerve-an integrative interface between two supersystems: the brain and the immune system. *Pharmacol Rev*. 2000;**52**(4):595-638. [PubMed: [11121511](https://pubmed.ncbi.nlm.nih.gov/11121511/)].
30. Reich M, Lesur A, Perdrizet-Chevallier C. Depression, quality of life and breast cancer: a review of the literature. *Breast Cancer Res Treat*. 2008;**110**(1):9-17. doi: [10.1007/s10549-007-9706-5](https://doi.org/10.1007/s10549-007-9706-5). [PubMed: [17674188](https://pubmed.ncbi.nlm.nih.gov/17674188/)].
31. Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. *Psychosom Med*. 2003;**65**(4):571-81. [PubMed: [12883107](https://pubmed.ncbi.nlm.nih.gov/12883107/)].
32. Kuhn TS, Hacking I. The structure of scientific revolutions. Chicago: University of Chicago press; 2012.
33. O'Connell WE. Frankl, Adler, and spirituality. *J Relig Health*. 1972;**11**(2):134-8. doi: [10.1007/BF01533215](https://doi.org/10.1007/BF01533215). [PubMed: [24414682](https://pubmed.ncbi.nlm.nih.gov/24414682/)].
34. West W. Psychotherapy and Spirituality: Crossing the Line Between Therapy and Religion. London: SAGE Publications; 2000.
35. Basu S, Nagy JA, Pal S, Vasile E, Eckelhoefer IA, Bliss VS, et al. The neurotransmitter dopamine inhibits angiogenesis induced by vascular permeability factor/vascular endothelial growth factor. *Nat Med*. 2001;**7**(5):569-74. doi: [10.1038/87895](https://doi.org/10.1038/87895). [PubMed: [11329058](https://pubmed.ncbi.nlm.nih.gov/11329058/)].
36. Nazlican E, Akbaba M, Okyay RA. Evaluation of depression in newly diagnosed breast cancer cases in Hatay province of Turkey in 2011. *Asian Pac J Cancer Prev*. 2012;**13**(6):2557-61. [PubMed: [22938420](https://pubmed.ncbi.nlm.nih.gov/22938420/)].
37. Missale C, Nash SR, Robinson SW, Jaber M, Caron MG. Dopamine receptors: from structure to function. *Physiol Rev*. 1998;**78**(1):189-225. [PubMed: [9457173](https://pubmed.ncbi.nlm.nih.gov/9457173/)].
38. Terasaka H, Tamura A, Takayama F, Kashimata M, Ohtomo K, Machino M, et al. Induction of apoptosis by dopamine in human oral tumor cell lines. *Anticancer Res*. 2000;**20**(1A):243-50. [PubMed: [10769662](https://pubmed.ncbi.nlm.nih.gov/10769662/)].
39. Gutzkow KB, Lahne HU, Naderi S, Torgersen KM, Skalhogg B, Koketsu M, et al. Cyclic AMP inhibits translation of cyclin D3 in T lymphocytes at the level of elongation by inducing eEF2-phosphorylation. *Cell Signal*. 2003;**15**(9):871-81. [PubMed: [12834812](https://pubmed.ncbi.nlm.nih.gov/12834812/)].
40. Jacobs JR, Bovasso GB. Early and chronic stress and their relation to breast cancer. *Psychol Med*. 2000;**30**(3):669-78. [PubMed: [10883721](https://pubmed.ncbi.nlm.nih.gov/10883721/)].
41. Pornour M, Ahangari G, Hejazi SH, Deezagi A. New perspective therapy of breast cancer based on selective dopamine receptor D2 agonist and antagonist effects on MCF-7 cell line. *Recent Pat Anticancer Drug Discov*. 2015;**10**(2):214-23. [PubMed: [25876608](https://pubmed.ncbi.nlm.nih.gov/25876608/)].