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Immune system and epigenomics under the light of spirituality/religiosity: a concise systematic review

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Abstract

Introduction: In the scenario of spirituality, immunity, and health, psychological science is considering spirituality/ religiosity (S/R) as a legitimate issue in understanding the human experience, as it can reduce pro-inflammatory cytokines, aberrant DNA methylation, and strengthen immunity. Objective: It was to evaluate the results of clinical studies that addressed the influence of spirituality/ religiosity on the human immune system, gene expression, and health in general. Methods: The systematic review rules of the PRISMA Platform were followed. The search was carried out from October to December 2022 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases, using articles from 2005 to 2022. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed accordingly. according to the Cochrane instrument. Results and Conclusion: A total of 120 articles were found, 55 articles were evaluated in full and 31 were included and developed in this systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 15 studies with a high risk of bias and 32 studies that did not meet GRADE. Results and Conclusion: Spirituality/religiosity plays an important role in epigenomic modulations, given that altered gene transcription and aberrant DNA methylation were observed in the CNS and peripheral T lymphocytes. Church attendance is associated with less herpesvirus reactivation, as indicated by lower levels of CMV IgG antibody titers. Furthermore, better self-reported health was associated with better functioning of the immune system. Spirituality can be considered a good coping strategy used by health professionals to promote mental health, well-being, and strengthening immunity during the COVID-19 pandemic.

Keywords: Spirituality. Religiosity. Immune system. Gene expression. Epigenomics.

Introduction

In the scenario of spirituality, immunity, and health, psychological science is considering spirituality/ religiosity (S/N) as a legitimate issue in understanding the human experience. To a large extent, this renewed interest was motivated by the positive association between this variable and physical and mental health. In this regard, it is necessary to develop a rationale for how various physiological mechanisms may mediate the effect of S/R on health [1].

In this sense, one of the greatest transformations in religion in contemporary societies has been the decline of church institutions and their reconstruction within a diverse network of associations, therapies, markets, and other unconventional spiritual services [1]. Religious and spiritual beliefs have long been used to deal with difficult situations, and it is necessary to adopt S/N in physical and mental health during the COVID-19 pandemic since previous studies seem to support its role in favorable health outcomes [2].

In this context, with the challenges in understanding the multifactorial etiologies of diseases and the heterogeneity of the effect of individual treatment in the last four decades, much has been learned about how the physical, chemical, and social environments affect human health, predisposing certain subpopulations to adverse outcomes from health, especially the socio-environmental disadvantaged. Current translational data on genetic interaction and adverse environment have revealed how adverse gene-environment interaction, termed aberrant epigenomic modulation, translates into impaired gene expression through dysregulation of messenger ribonucleic acid

(mRNA), reflecting abnormal protein synthesis and therefore dysfunctional cell differentiation and maturation [3].

Therefore, the environmental influence on gene expression observed in most of the literature includes the physical, chemical, physical-chemical, and recent social environment. However, data are limited on spiritual or religious environment network support systems, which reflect human psychosocial conditions and gene interaction. Adverse human psychosocial conditions are prone to impaired gene expression through an upregulated transcriptional adversity response gene expression that is upregulated via social signal transduction, involving the sympathetic nervous system (SNS), beta-adrenergic receptors, the hypothalamic-pituitary-adrenal (HPA) axis, and the glucocorticoid response. While still in need of further investigation into psychosocial and immune cell response and gene expression, current data in human models reveal that appropriate gene expression through the upregulated transcriptional adversity response and NR3C1 gene in the spirit network support system, as seen in meditation, yoga, and Thai-chi enables the remission of malignant neoplasms [3].

Furthermore, social networking that entails enhanced parenting skills, family interactions, and individual capacity development has been shown to improve health outcomes, while disruption of social networking induces poor health outcomes as well as decreased pro-inflammatory cytokines [1]. Previous studies have looked at how the DNA methylation profile differentiates these types of happiness, resulting in better health outcomes with self-transcendence driven by altruism [4,5]. With the observed data on differential DNA methylation and correlated health outcomes and the observation of a spiritual network support system as a positive social interaction and antithesis to social isolation and unstable social status, there is a need to examine how the system Spiritual network support enhances human gene expression, health status, prognosis, and survival. Understanding how social conditions, such as the spiritual support network system, influence the biological process in the pathophysiological mechanism of cause and prognosis of the disease, allows the characterization of specific risks and mapping of reliable intervention with the identification of biomarkers and implementation of policies social [4].

Therefore, the present study aimed to evaluate the results of clinical studies that addressed the influence of spirituality/ religiosity on the human immune system, gene expression, and health in general.

Methods

Study Design

This was followed by a systematic literature review model on the main clinical findings of mandible fractures, according to the PRISMA rules (Transparent reporting of systematic review and meta-analysis-HTTP://www.prisma-statement.org/).

Data sources and research strategy

The literary search process was carried out from September to November 2022 and was developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, using scientific articles from 2005 to 2022, using the descriptors (MeSH Terms): “Spirituality. Religiosity. Immune system. Gene expression. Epigenomics", and using the Booleans "and" between the descriptors (MeSH Terms) and "or" between the historical findings.

Study quality and risk of bias

The quality of the studies was based on the GRADE instrument, with randomized controlled clinical studies, prospective controlled clinical studies, and studies of systematic review and metaanalysis listed as the studies with the greatest scientific evidence. The risk of bias was analyzed according to the Cochrane instrument.

Results and Discussion

Summary of Literary Findings

A total of 120 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 102 articles. A total of 55 articles were evaluated in full and 31 were included and developed in this systematic review study (**Figure 1**). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 15 studies with a high risk of bias and 32 studies that did not meet GRADE.

Figure 2 presents the results of the risk of bias in the studies using the Funnel Plot, through the calculation of the Effect Size (Cohen's Test). The sample size was determined indirectly by the inverse of the standard error. The number of clinical studies evaluated was n=31. The graph showed symmetric behavior, not suggesting a significant risk of bias in studies with small sample sizes, which are shown at the bottom of the graph.

Figure 1. Selection of studies.

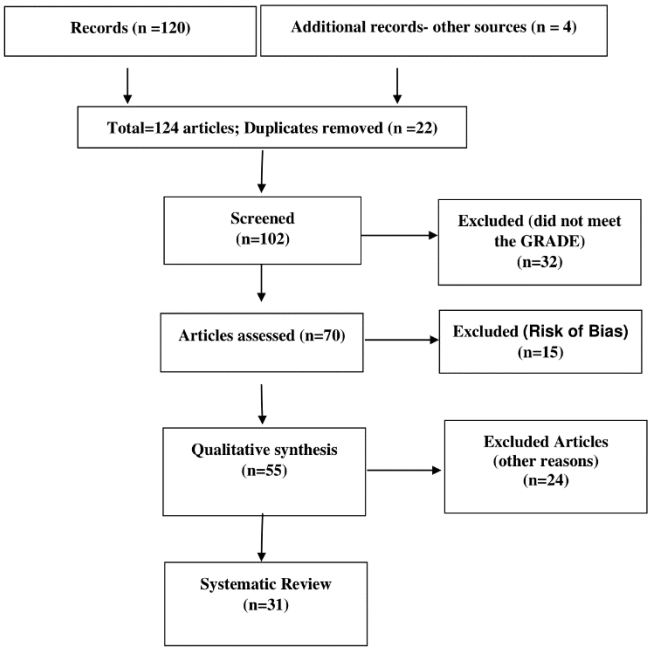
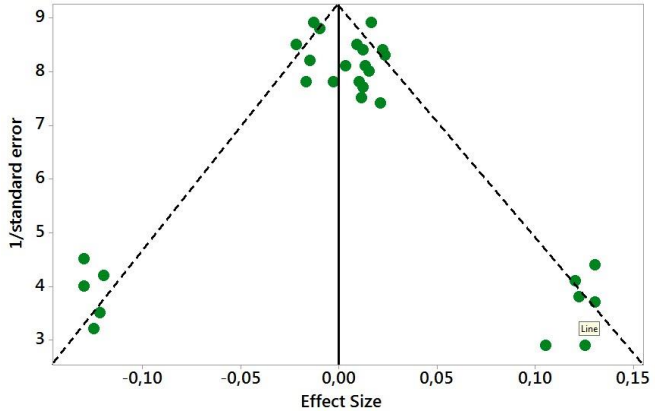


Figure 2. The symmetric funnel plot does not suggest a risk of bias between the small sample size studies that are shown at the bottom of the graph (N=31 studies).



Source: own authorship

Main Clinical Outcomes - Spirituality/Religiosity (S/R) in Immunity and Health

S/R has been increasingly highlighted in the current sports environment, proving to be closely related in a positive and altruistic way, impacting the improvement of the immune system, as well as better health recovery [1]. Individuals who regularly participate in spiritual worship services or related activities and who feel strongly that spirituality or the presence of a higher being or power are sources of strength and comfort to them are healthier and have greater healing abilities. Numerous research investigations have reported positive correlations between spirituality and reduced rates of stroke, cancer, cardiovascular disease, hypertension, substance abuse, suicide, and overall mortality. It has been suggested that faith is beneficial for health and healing because it helps people avoid harmful behaviors such as smoking and excessive drinking [6].

In this sense of the immune response and S/N, a study developed by Garcini et al. 2019 investigated the association between church attendance and cytomegalovirus (CMV) latency by assessing CMV IgG antibody titers among bereaved and non-bereaved individuals. Participants were 44 mourners and 44 controls with a mean age of 68 years (SD=12.84). After adjusting for participant age, sex, education, minority status, weekly alcohol consumption, smoking, depression, body mass index (BMI), and comorbidities, church attendance was associated with lower CMV IgG antibody titers among participants mourners, and controls. In addition, there was a significant moderating effect of church attendance on the association between bereavement and CMV IgG antibody titers, such that church-attending bereaved individuals had less herpesvirus reactivation (lower antibody titers CMV IgG) when compared to non-church-going bereaved [7].

Furthermore, a study examined the relationship between religiosity and the affective and immunological status of 106 slightly symptomatic HIV-seropositive gay men. Factor analysis of 12 religious orientation response items revealed two distinct aspects of religiosity: religious coping and religious behavior. Religious coping (eg, putting trust in God, seeking comfort in religion) was significantly associated with lower scores on the Beck Depression Inventory, but not with specific immunological markers. Religious behavior, on the other hand, showed that the associations of religiosity with the affective and immunological state were not mediated by the subjects' sense of self-efficacy or ability to actively deal with their health situation. Associations between religiosity and affective and immunological status also appear to be independent of symptom status. Selfefficacy, however, seems to contribute uniquely and significantly to decreasing depression scores [8].

As a corollary of this, a spiritual network system reflects the structure organized by individuals or groups with the notion of transcendence based on hope, faith, and divine providence, indicative of a supernatural aspiration. This concept is perceived as a social condition and plays an important role in epigenomic modulations [9]. Neurophysiological changes have been associated with social stress due to the disruption of the social environment. Studies on social stressors implicate epigenomic mechanisms in the translation of social stressors such as isolation and a state of psychosocial wellbeing into biological and physiological adaptation. Specifically, available data on early life stress (ELS) due to parenting deficits in infancy and childhood correlate inversely with physiological stability and normal health

[10]. Furthermore, psychological trauma and social isolation with prolonged or sustained exposure result in aberrant epigenomic modulation and related adverse health outcomes. Prolonged stress impairs this adaptive mechanism, resulting in allostatic overload and therefore ineffective adaptation, physiological change, and poor health outcomes [11].

An example of social stressors such as ELS has been illustrated in pre-and postnatal stress and maternal care inadequacies associated with behavioral pathologies [12-14]. In general, the main neural substrates involved in the epigenetic modulation of ELS and maternal care include HPA, the amygdala, the medial prefrontal cortex, and the hippocampus region of the brain. The phenotypes observed in aberrant epigenomic modulation in ELS are explained by the downregulation and downregulation of the NR3C1 gene, a glucocorticoid receptor (GR) gene.

In this regard, prolonged activation of the HPA axis, altered gene transcription, and aberrant DNA methylation have been observed in the CNS and peripheral T lymphocytes among infants and young adults deprived of maternal care [15-20]. Aberrant epigenomic (mDNA) and hydroxymethyl cytosine modulation at the brain-derived neurotrophic factor (BDNF) locus, a member of the neutrophil nerve growth factor family, has been observed in adolescence and adult distress associated with maternal maltreatment during pregnancy neonatal breastfeeding of the offspring. Other neural changes include the hippocampus, amygdala, and medial prefrontal cortex [21-24]. Later studies observed increased expression of arginine vasopressin (AVP) and gene loci, a protein-coding gene for antidiuretic hormone (vasopressin) associated with diabetes insipidus, and DNA hypomethylation in the paraventricular nucleus of the hippocampus in ELS, due to maternal separation. Likewise, overexpression of the proopiomelanocortin (POMC) gene loci, which is involved in the production of adrenocorticotropic hormone (ACTH) and binds to the melanocortin 2 receptor (MC2R), stimulating the release of cortisol, is observed in ELS associated with maternal separation [25,26].

Gene expressions are implicit in behaviors or activities associated with religious beliefs and cults contrary to social adversity that result in impaired gene expression. Despite sparse data on epigenomic modulation in Christian, Islamic, and Hindu religions, observed behavior in these religions reflects potentials for the DNA methylation process that can signal appropriate gene expression, enhance cellular activities, and optimize health outcomes. Indeed, given the role of social network systems in human health and the implication of religious and spiritual activities in this context, there is a tendency to consider how spiritual activities could improve human gene expression due to normal epigenomic modulation via methylation processes of the DNA involved in the expression of the upregulated transcriptional adversity response and NR3C1 genes [3].

Added to this, a study carried out by the author's Warner et al. 2020 looked at whether childhood and/or adolescent abuse was associated with shorter telomere length in a pooled analysis of 3,232 participants from five diverse cohorts, as well as assessing whether S/R could buffer the deleterious effects of abuse. Compared with no abuse, severe sexual abuse was associated with lower leukocyte relative telomere length (LRT) z-scores, childhood: -15.6%, 95% CI: -25.9, -4.9; p-trend = 0.04; p-heterogeneity = 0.58 and in adolescence: -16.5%, 95% CI: -28.1, -3.0; p-trend = 0.08; pheterogeneity = 0.68. Childhood and adolescent sexual abuse was associated with 11.3% lower LRT z scores after adjusting for childhood and demographic covariates (95% CI: -20.5%, -2.0%; p- trend = 0.03; p-heterogeneity = 0.62). The lack of moderation by S/R may be due to the inability to capture the appropriate period for these beliefs and practices [27].

Also, a study evaluated whether the relationship between stress and health was mediated by the meaning of life. Based on Wave 1 of the Landmark Spirituality and Health Study, a nationally representative sample of adults, participants (N=1871) reported their stress level in the last 12 months, the current meaning of life, and health and provided a blood sample for biomarker immune system function (i.e., presence of Epstein-Barr virus antibodies). The results revealed a model of indirect effects in which stress was inversely associated with meaning. Higher significance was related to better self-reported health which, in turn, was associated with better immune system functioning [28]. The author's Kes et al. 2013 argued that quality of life (QoL) in patients with multiple sclerosis is a multidimensional construct composed of functional, physical, emotional, social, and spiritual wellbeing. Individuals with multiple sclerosis have a lower quality of life than non-ill and diseased populations. The inclusion of quality-of-life questionnaires in patient follow-up is a relevant issue to optimize treatment, facilitate therapeutic decisions and improve adherence, as well as reduce medication-related inconveniences. In this sense, S/R plays an extremely important role in regulating the immune system, as well as improving the quality of life of these patients [29].

Finally, coronavirus disease 2019 (COVID-19) has presented unprecedented health challenges across all strata of society across the world. The COVID experience made us reflect on the quality of life, health

and well-being, and, just as important, the end of life. During this period, spiritual care constitutes a vital component of holistic health management, especially in terms of coping, coping with illness, suffering, and ultimately death. While spiritual care has always been part of the realm of religious beliefs, a more contemporary perspective is that spiritual care is part of the human psyche and therefore part of human care, health, and well-being for families, patients, and healthcare professionals. health. Spiritual care deals with providing compassion and empathy during periods of heightened stress, distress, and anxiety within care by regulating the immune system [30]. Previous studies have indicated that spirituality in these times of crisis serves as a source of hope and wellbeing that helps people get through the day. Another study investigated the role of S/R in health during the COVID-19 pandemic. The findings revealed the importance of including spirituality in clinical practice for both health professionals and patients. On the one hand, spirituality can be considered a good coping strategy used by health professionals to promote mental health, well-being, and strengthening immunity during the COVID-19 pandemic. Still, addressing the spiritual needs of individuals leads to reduced stress, anxiety, and depression and increased resilience and hope in patients [31].

Conclusion

Spirituality/religiosity plays an important role in epigenomic modulations, given that altered gene transcription and aberrant DNA methylation were observed in the CNS and peripheral T lymphocytes. Church attendance is associated with less herpesvirus reactivation, as indicated by lower levels of CMV IgG antibody titers. Furthermore, better self-reported health was associated with better functioning of the immune system. Spirituality can be considered a good coping strategy used by health professionals to promote mental health, well-being, and strengthening immunity during the COVID-19 pandemic.

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Ethics approval

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Informed consent

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate@.

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