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Psychoneuroimmunology and oncology nursing: a theoretical study

Psiconeuroimunologia e a enfermagem oncológica: estudo teórico

Psiconeuroinmunología y la enfermería oncológica: estudio teórico

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ABSTRACT

Objective: To discuss the evolution of research in cancer psychoneuroimmunology, the advances in the management of neuropsychological symptom clusters and their interface with mid-range theories, and practical applications in Nursing. **Method:** This is a theoretical-reflective study anchored in recent literature, as well as in the critical analysis of the authors. **Results:** This is a promising field of investigation, which emphasizes the complexity and interaction of symptoms, the interrelationships among them, the factors influencing them, and their consequences. Subsidized by mid-range theories in Nursing, such as the Theory of Unpleasant Symptoms and the Theory of Symptom Management, analyses of these interrelationships support Oncology Nursing diagnoses and interventions. **Conclusion:** An innovative approach is proposed to qualify Oncology Nursing care based on the integration of recent advances in cancer psychoneuroimmunology, Nursing mid-range theories, and practical tools such as health coaching. The approach proposed may strengthen clinical nursing practice in the management of neuropsychological symptom clusters in oncology and shall be integrated into decision-making during cancer treatment, favoring person-centered care.

DESCRIPTORS

Psychoneuroimmunology; Oncology Nursing; Concurrent Symptoms; Neuroimmunomodulation; Neoplasms; Mentoring.

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INTRODUCTION

As from the time of Hippocrates, there has been debate on the assumption that the biological adjustment to endogenous or exogenous insults, related to emotions and diseases, would be the result of an intrinsic and articulated system in which each of the parts would evolve to perform a specific function.[1] However, in recent decades, this adaptation has been understood because of research and advances arising mainly from the fields of molecular biology, genetics, and neurosciences, which have contributed to a better comprehension of the communication pathways among the nervous, endocrine, and immune systems.[1–2]

The physiological mechanisms involved in the regulation of the nervous, endocrine, and immune systems were, for a long time, one of the main foci of biomedical research. However, until recently, they were studied in an isolated and fragmented way. Then, the establishment of integration of the complex relationships among these systems[2] was tried. In this context, the term "Psychoneuroimmunology" (PNI) was introduced in the 1970s[1], to "*designate the field of science that studies, in an interdisciplinary way, the interaction between psychological processes and neurological, endocrine, and immunological functions, and their influence on health*"[2]. It should be noted that a growing body of research involving PNI has provided strong evidence and new insights that support the understanding that numerous and complex interactions between insults/physical stressors, as well as those of a social, psychological, and spiritual order, can modulate the immunological response through psychoneuroimmunoendocrine pathways[2].

This article aims to: i) identify the impact of the progression of research in the field of cancer psychoneuroimmunology; ii) present the current panorama of advances in the field of neuropsychological symptom clusters management, and iii) discuss its interface with Oncology Nursing theories and practice.

METHOD

This is a theoretical-reflective study, whose rationale is based on the discursive formulation about the theme, supported by national and international scientific literature and critical analysis of the authors. Based on the theoretical construction of reflective thinking[3], historical and conceptual aspects of the evolution of the term sickness behavior to neuropsychological symptom clusters in Oncology were addressed, and the interface of studies involving PNI with Oncology Nursing theories and practice was elucidated.

Stress from the Perspective of Cancer PNI

Stress is associated with numerous pathologies, including cancer, and exerts an immunosuppressive effect[4]. The physiological stress manifested with the progression of the disease suppresses important facets of the immune response, such as the activity of Natural Killer (NK) cells and the proliferation of T cells, cells that play an important role in the immune response against cancer[4]. Exposure to a stressor(s) activates the hypothalamic-pituitary-adrenal (HHA) axis to release catecholamines (norepinephrine and epinephrine) through the sympathetic nervous system. Moreover, it activates neurons in the paraventricular nucleus of the hypothalamus, which secrete corticotropin-releasing hormone. This hormone acts on the anterior pituitary promoting the release of adrenocorticotropic hormone, which acts on the cortex of the adrenal gland, initiating the synthesis and release of glucocorticoids[4–5].

Cortisol release follows a circadian pattern, in which this hormone is normally secreted by the adrenal gland in short bursts, with 15 to 30 pulses over a day[4]. Peripheral cortisol levels, measured in blood or saliva, reflect the activity of the HPA axis and can be used as a biomarker to assess responses to stressful stimuli or to determine the effectiveness of interventions to reduce stress[4]. High concentrations of cortisol inhibit antigen presentation, lead to atrophy of the lymphoid tissue of the thymus, spleen, and lymph nodes, besides stimulating programmed cell death (apoptosis) of lymphocytes. Additionally, increased levels of this glucocorticoid inhibit the synthesis and release of cytokines and other mediators of immune and inflammatory reactions[4–5]. Cortisol, in high concentrations, also modifies the balance between the cellular immune response (Th1), important in the defense against cancer, and the humoral (Th2) response, towards the Th2 response[4–5]. These changes are associated with a decrease in the cytotoxic activity of lymphocytes and NK cells, favoring, among others, the evasion of the antitumor immune response. Disruption of the immune balance can also lead to a chronic cascade of events mediated by pro-inflammatory cytokines (IL-1β, IL-6, TNF-α and IFN), resulting in stress feedback loop, depression, anxiety, cancer-related fatigue (CRF), sleep disorders, cognitive alterations, and subsequent negative impact on quality of life[5–6]. Results from clinical trials have suggested that pro-inflammatory cytokines modulate the effects of a variety of physical and psychological stressors, and increased concentrations of these molecules have been related to worsening in health-related quality of life[7–8]. Briefly, stress, through the activation of the neuroimmunoendocrine axis, can negatively influence multiple biological pathways of carcinogenesis, from the onset and progression of neoplasia to metastases[7–8].

From Sickness Behavior to Neuropsychological Symptom Clusters in Oncology

Tumor progression and anticancer therapy can result in the manifestation of numerous symptoms during and even after patient treatment, including CRF, sleep disorders, cancer pain, cognitive dysfunction, anxiety, among others. These symptoms reduce the individual's functional status, with consequent decrease in quality of life, and may occur alone or together, constituting clusters of symptoms[6,9]. The term cluster is defined as a conglomeration of inter-related and predictable symptoms[6]. The current challenge for exploring these clusters of symptoms is to clearly demonstrate the meaning of the cluster in terms of interaction, patterns of association, and synergy. The first studies involving clusters of neuropsychological symptoms stem

from experiments with mice subjected to the induction of infectious conditions and the injection of pro-inflammatory cytokines in their hind legs. Thus, a pattern of neuropsychological symptoms cluster was observed for the first time from the moment these animals showed infectious and inflammatory conditions through inductions, which culminated in the phenomenon of "sickness behavior"[6–7].

The term sickness behavior was established in 1992[10], to designate a set of behavioral changes occurring with diversified pathological and inflammatory processes. The authors also referred to some behaviors changed during the course of these diseases, such as the apparent loss of interest of these animals in daily activities (search for food, decreased social interaction, and sexual interest)[10].

Therefore, the history of sickness behavior was primarily derived from studies of the effects of bacterial products on this "sickness behavior". LPS, a gram-negative bacterial wall lipopolysaccharide, is described as one of the main bacterial products analyzed in these processes[11]. The effects of pro-inflammatory cytokines, such as interleukins IL-1β, and IL-6, whose roles in inflammatory processes have been well reported in the literature, were also analyzed[11–12].

Studies in animals and humans have shown that the infusion of cytokines (systemically or centrally) also induces the phenomenon of sickness behavior. The same symptoms are described in volunteers injected with molecules that induce the synthesis of endogenous cytokines, such as lipopolysaccharides[1]. Thus, in a very similar way to the phenomenon of sickness behavior, presented by laboratory animals, in humans, especially in cancer patients, cancer pain, CRF, cognitive and sleep disorders, anxiety, and depression associated with high levels of expression of pro-inflammatory cytokines found were observed[6,11–12]. The establishment of sickness behavior in cancer patients culminated in the appearance of a new concept, the "neuropsychological symptom cluster" – which is defined as "a set of emotional and/or behavioral symptoms that may be related to psychological and/or neurological dysfunction and that has a tendency to occur in cancer patients"[6,13–14].

There is a growing consistency that common biological mechanisms may underlie the interaction among the nervous, endocrine and immune systems, which orchestrate a set of responses capable of installing behavioral and physiological changes in the animal and human organism[11–13]. In particular, studies addressing the sickness behavior, as well as the neuropsychological symptom clusters in cancer patients, support the hypothesis that pro-inflammatory cytokines are related to the biological mechanisms underlying the emergence of these symptom clusters[9,11]. The release of cytokines such as IL-1β, IL-6, IL-8, TNF-α, IL-12p70 and IFN-y, for example, results in neuropsychological symptoms clusters, including depressed mood, CRF, depression, sleep disorders, and increased sensitivity to pain. Changes in cytokines and other neuroimmunological processes can be critical for the production of symptoms and, potentially, can be considered a target for their prevention and treatment[5–7,12–14].

In the tumor microenvironment, cytokines stimulate the host's response to control cell stress and reduce cell damage[15]. Pro-inflammatory cytokines (IL-1β, IL-6 and TNF-α) are closely associated with the pathophysiology of CRF, as well as with sleep disorders[5–6]. A study comprising a sample of 28 women with breast cancer, at different stages of the disease, found that high concentrations of the IL-1 receptor antagonist (IL-1ra) were correlated with high levels of CRF ($p < 0.03$)[16].

Evidence supports a strong association among depression, anxiety, cachexia, and high levels of expression of the cytokines IL-1β, IL-6, IL-10, TNF-α, INF-γ and fractalkine (CX3X) in cancer patients.[6,11–12] These signaling proteins are essential mediators and play a central role in the immune response directed at tumors, since they are intrinsically associated with the process of carcinogenesis in the tumor microenvironment, acting both in signaling tumor growth and in the development of metastases[15]. Studies have shown that alterations in genes encoding pro-inflammatory cytokines (IL-1β, IL-6), and their high concentrations, greatly contribute to the occurrence, intensity, and severity of various symptoms in cancer patients[16–17]. Researchers have demonstrated an association among polymorphisms in genes encoding IL-1β and IL-6, and CRF. The CRF predictors included the presence of at least one cytokine in the IL1β-511 allele (95% CI = 0.91–16.6, $p = 0.007$) and homozygosity for any variant of the IL6-174 genotype (G/G or C/C; 95% CI = 1.12–17.9, $p = 0.027$)[17].

Single Nucleotide Polymorphisms (SNP) of IL-1β, IL-10, and TNFR2 have contributed to the identification of patients at high risk for a given set of symptoms. In a study carried out with 599 patients recently diagnosed with lung cancer, it was found that, in the 55 polymorphisms analyzed, an additive effect of the mutant alleles of IL-1β, IL-10 and TNFR2 genes were predictive for the severe pain, depressed mood, and CRF cluster in these patients. Furthermore, SNPs in the IL-10 coding gene were correlated with a significantly increased risk for CRF, that is, women with the Lys/Glu genotype had 0.49 times less risk of severe CRF than those women with the genotype Lys/Lys (OR = 0.49, 95% CI = 0.25–0.92, $p = 0.027$)[18].

In this scenario, PNI has contributed to the identification of possible mechanisms underlying the cancer symptom clusters, which can be used as a framework to assess the neurobehavioral toxicity of anticancer therapies, particularly in patients who are at higher risk of symptom severity[9,14].

PNI and Oncology Nursing: Impact on Research and Professional Practice

Until recently, research on PNI carried out by Nursing professionals was relatively limited. As nurses seek training as researchers and join research teams in areas of basic science, they also become more aware of the projections and clinical impact of psychoneuroimmunological approaches[7,9]. The result of these collaborations is a synergistic growth in translational and interdisciplinary research focused on the fusion of the biological, psychological, and sociocultural

dimensions of patient care, aiming at improving patient health outcomes[9]. Some works, considered a landmark of PNI, researched by Nursing in Brazil, are discussed here.

A groundbreaking work in the field of Psychoneuroimmunology and Oncology Nursing in Brazil, from 1998[19], evaluated the effect of a relaxation-nursing intervention on the immune system in women with breast cancer. Two groups of women with breast cancer without metastases and undergoing surgery were compared, the activity of NK cells (Natural Killer) was investigated as an immunological parameter, and the behavior patterns for stress, coping, and anxiety in these patients were assessed. The results showed that relaxation modulated and increased NK activity of the immune system in the experimental group[19].

Another study[20] assessed the expression of cytokines IL-1β, IL-6, IL-8, IL-10, TNF-α, IL-12p70 and correlated them with CRF, sleep pattern, and health-related quality of life (HRQOL) in pediatric cancer patients. A negative correlation was evidenced between the scores of general fatigue and IL-1β. Sleep efficiency and duration were positively correlated with IL-10. A negative correlation was also observed between IL-1β and the total HRQOL score, indicating that increased levels of IL-1β result in decreased HRQOL[20].

More recently, quasi-experimental studies[21–22] have investigated the effects of clowns intervention on psychological stress and CRF in pediatric cancer patients undergoing chemotherapy. In this study, eight samples of saliva were collected in the pre-intervention and eight in the post-intervention at defined times (+1h, +4h, +9h and +13h after awakening). The concentrations of salivary cortisol, sAA (salivary alpha-amylase), pro- and anti-inflammatory cytokines, and matrix metalloproteinases-9 (MMP-9) were measured, while stress and CRF were evaluated by validated scales (Children's Stress Scale – ESI™ and Multidimensional Fatigue Scale-PedsQL™, respectively). It was observed that the levels of total psychological stress, as well as the general fatigue of pediatric cancer patients, improved significantly after the intervention. In addition, IL-1β and cortisol levels were shown to be reduced in these patients. There was also a positive correlation between IL-1β, cortisol, and sAA cytokine levels after the intervention. These results suggest that hospital clowns can be used as a non-pharmacological intervention to reduce psychological stress and CRF in pediatric cancer patients undergoing chemotherapy[21–22].

The results of scientific investigations carried out by nurses, in the light of basic sciences, are benchmark for personalized care[9]. Thus, it is important for nurses to participate and identify strategies to accelerate translational investigation, based on the professional practice scenario, to assist in understanding the underlying pathophysiological mechanisms associated with these symptoms, aiming at intervening effectively[9,20]. Above all, nurses are in an ideal position to develop personalized interventions because, notoriously, they are the professionals who are on the frontlines of care, providing uninterrupted care to patients. These aspects support the Evidence-Based Practice, favoring the scientific autonomy of the care provided by these professionals, providing subsidies for qualified assistance. However, the PNI still occurs in a very incipient way in the Brazilian nursing universe[7,9].

Research on the PNI area has the potential to validate aspects of care that nurses intuitively use for the benefit of their patients, and supports the implementation of the use of complementary therapies in nursing practice[7]. Consequently, research to assess the effectiveness of nursing interventions, if designed based on the perspective of PNI, will allow nursing researchers to investigate which bio-behavioral processes are closely intertwined and need to be considered in the provision of patient care to help them with quality and safety in their therapeutic itineraries[7,9,20].

Currently, one of the emerging themes for Oncological Nurses is the management of cancer-related neuropsychological symptoms clusters[2,9,13]. In general, research in Oncology concentrates preferentially on the prevalence of symptoms analyzed in isolation, instead of considering them as concomitant symptoms that form clusters. However, professional practice shows us that symptoms rarely occur separately, but rather form clusters that even share common underlying mechanisms in terms of intensity and severity, creating a synergistic effect among them, or a predecessor effect, which can predict the development of future symptoms[2,6–7,9,13].

Nurse researchers shall be aware of and sensitized to the patients' experience of these unpleasant symptoms. Their study generates wealthy research opportunities, such as: a) the trajectory, development, and severity of these symptoms over time (treatment and post-treatment); b) the interrelationships between these symptoms, considering age group, sociocultural and spiritual aspects, diagnosis, and treatment phase; and c) which factors contribute to the formation of clusters among symptoms[9]. There is also great potential for the advancement of Nursing through research that assesses the psychoneuroimmunoendocrine pathways involved in the genesis of these symptom clusters. Once the association between symptoms and the degree of sensitivity and specificity of appropriate biomarkers is identified, they can be used to accurately assess the effectiveness of nursing interventions. Once these relations are established, it will be possible to predict in which context – which practices, for which patients, at which stage of the disease and treatment – interventions will have a greater chance of promoting clinical benefit[7,9,13,20].

Nursing and PNI Theories: Subsidies for Symptom Management

It is a consensus that in cancer patients, symptoms usually occur simultaneously, forming clusters that may share similar mechanisms[2,6,9,12]. The Middle-Range Theory of Unpleasant Symptoms (TOUS) is based on the premise that there is a multiplicative and integrated association of symptoms. TOUS was developed and introduced in 1995, through a joint effort of research nurses engaged in clinical practice[23]. TOUS proposes that some of the common factors can influence the experience of a number of different

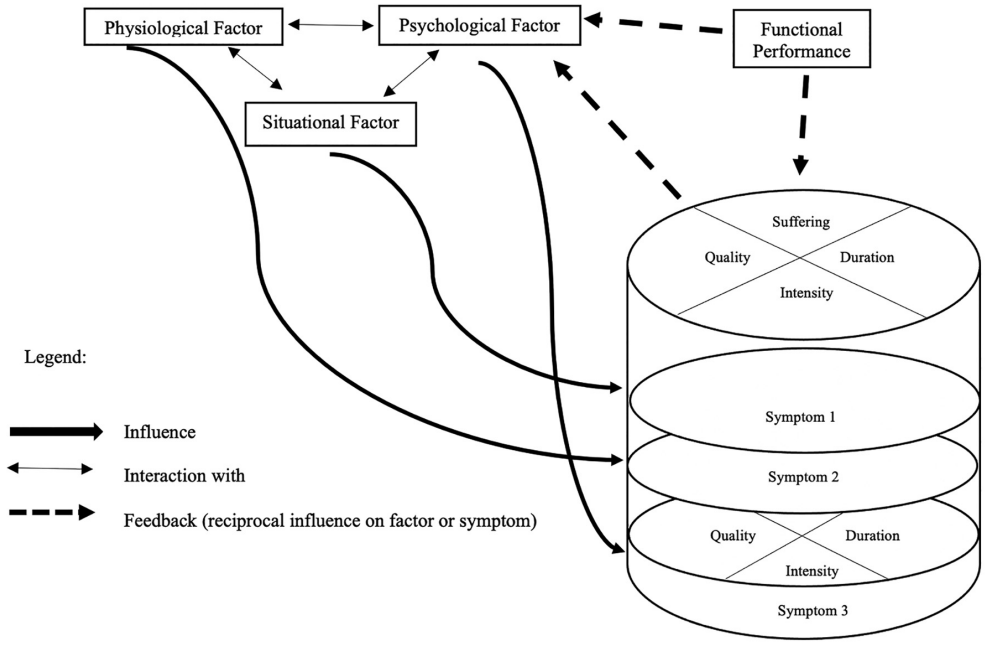

Figure 1 – Theory of unpleasant symptoms (TOUS)[23].

symptoms and, consequently, similar interventions can be effective in alleviating more than one symptom[23]. According to TOUS, a symptom would have a synergistic effect with others, impacting the intensity, occurrence, and severity of concomitant symptoms, and consequently, modulating the patient's HRQoL[23].

TOUS has three main components: the symptoms the individual is experiencing, the factors giving rise or influencing those symptoms, and the consequences of that experience. Each symptom is considered a multidimensional event and can be measured separately or in combination with others. Although symptoms are different from each other, there are common dimensions among them: intensity, time, degree of perceived suffering and of quality. In this theory, three factors influence these dimensions: physiological factors, psychological factors, and situational factors, responsible for the variability in the experiences of different individuals with similar symptoms[23–24] (Figure 1).

Among the physiological factors impacting the three dimensions common to unpleasant symptoms is the release of cytokines, for example, IL-1β, TNFα, IL-6, IL-8, IL-12p70, in addition to other cytokines and chemokines acting directly on the tumor microenvironment, thus inducing the appearance of concomitant symptoms. Furthermore, psychological, psychosocial and emotional factors, and situational factors such as the therapy used, are crucial for the emergence of these symptom clusters[6,9,12–13,24].

The synergy of physiological, psychological, psychosocial, emotional, and situational factors greatly influence the occurrence, intensity, severity, quality and duration of symptoms. Such synergy can culminate in a reduction in the patients' HRQoL, reflecting on both the determining factors for the appearance of these symptoms and on the symptoms themselves, working as a positive feedback for the incidence of multiple concomitant symptoms[23–24]. Thus, it is plausible to state that cancer symptom clusters are associated with clinical and prognostic worsening in cancer patients, as these patients tend not to cooperate and often postpone or even interrupt treatment. This results in an increase in the number of hospitalizations, high costs to health systems, the incidence of oncological emergencies, decreased functional capacity and, consequently, reduced HRQoL for these patients[23–24]. Unpleasant symptoms, their interaction, synergy, and complexity are experienced by patients under the care of nurses. TOUS encourages nurses to look at symptom constellations and propose appropriate interventions for patient-centered care[23–24]. By identifying a set of potential influencing factors, nurses find a structure in this theory to determine the extent of systems overlap, at a level of abstraction consistent with nursing diagnoses and interventions[23–24].

Another relevant mid-range theory is the Symptom Management Theory (SMT), whose assumptions lie in a multidimensional process of symptom management, with clinical applicability, especially in Nursing. In 1994, its first version was released at the University of California, San Francisco, and was called Symptom Management Model. The Symptom Management Model proposed at the time consisted of a deductive model for managing a symptom, focused on the process and contemplating the interaction of three components, namely: i) the experience of the symptom ii) the strategies for its management, and iii) the outcomes[25]. In 2001, already in the updated version of Symptom Management Model, the symptom management process presented an interface with some domains of Nursing Diagnoses. Later, in 2008, the Model was updated and renamed Symptom Management Theory and finally validated for use in Brazil[25–26] (Figure 2).

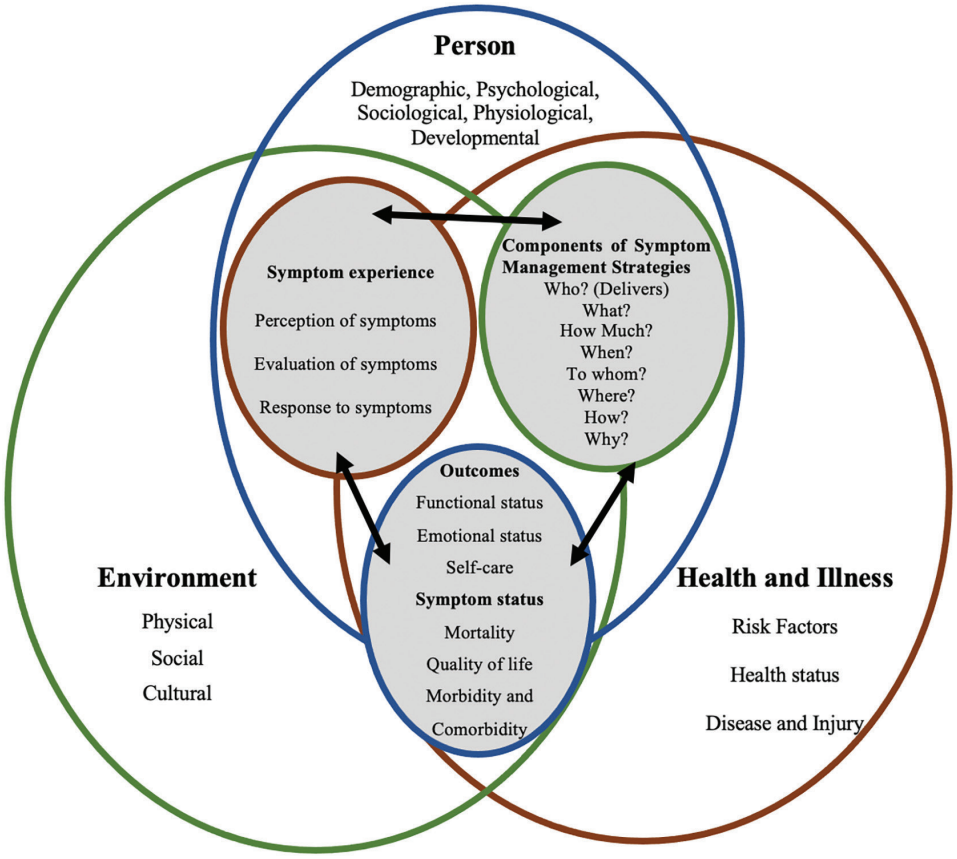

Figure 2 – Symptom Management Theory diagram.

The SMT is based on six hypotheses, namely: i) the gold standard for the study of symptoms is based on the perception and self-report of the individual presenting the symptom; ii) the symptom does not need to be experienced by an individual for this symptom management model to be applied – the individual may be at risk for developing a symptom due to the influence of a context variable, so that intervention strategies can be started even before an individual experiences a particular symptom; iii) for patients without verbal skills (babies and aphasic people), the interpretation of symptoms given by the immediate caregiver is assumed to be accurate for the purpose of implementing an intervention; iv) all unpleasant symptoms need to be managed; v) the management strategy can be directed to an individual, a group, a family, or to a work environment; vi) symptom management is a dynamic process, that is, modified by individual perceptions and by the influences of the Nursing domains, that is, the person, the environment, and the health-disease process[25].

The assumptions of the SMT lie in the fact that the proper management of a symptom or group of symptoms requires consideration of the three components of the Theory mentioned above (symptom experience, strategies for its management, and its outcomes), as well as the interrelationship among them[25]. It should be noted that the duration of symptom assessment depends on its occurrence, intensity and severity, as well as on the need for evolution/assessment of the interventions proposed. In this regard, when a symptom is successfully treated and resolved, the model is no longer relevant. However, if continued intervention is required to control symptoms that are co-occurring, the model persists and, therefore, shall be applied taking into account the implementation phase of the intervention followed by symptom assessment[24–25].

Due to its applicability both in research and in the professional practice settings, SMT has the potential to affect Oncology Nursing care positively. Such Theory provides a conceptual framework for better understanding of the intrinsic network of connections between the experience of a symptom and its associated situational factors that can influence its management. This way, SMT can guide Nursing interventions, specifically in what regards the effective management of cancer symptom clusters. Likewise, SMT is able to influence institutional practices and create timely care environments to resolve concomitant symptoms in an organizational context[24].

One of the most challenging issues for nurses today, both in research environments and in clinical practice, is the translation of Nursing theories for application in the context these professionals are inserted. Among the several ways of thinking about theoretical-practical issues, the experience of cancer symptom clusters, supported by mid-range Nursing theories, presents itself as an adequate and promising model. Researchers and nursing professionals

are turning their attention to biological mechanisms responsible for clinical conditions of chronic diseases as guiding instruments to propose effective interventions. The combination of theory and clinical experience has the potential to leverage the quality of nursing care. This integrated approach and exploration favor the development and implementation of new ideas that will be translated into new safe practices for health care[7,9,20,24–26].

Health Coaching as a Tool for Nurses in Managing Symptoms in Cancer Patients

Emerging in corporate organizations and with positive results in Psychology, sports, business and, more recently, in Nursing, coaching processes were adapted to promote changes in habits aiming to improve well-being and quality of life. It has been shown that health coaching is effective in encouraging, inspiring, and enabling patients to reach their maximum health potential, mainly through lifestyle changes[26]. This practice uses motivational interviewing and elements of cognitive-behavioral practices that promote self-knowledge and alignment of values in patients, enabling them to self-care.

Integrative Health Coaching is an emerging practice that has been systematized in the main American medical schools since 2000. This practice is centered on the person and not on the disease, based on evidence, and aims to follow people in their improvement of health and well-being[27]. Integrative Health Coaching uses techniques obtained from Humanistic and Positive Psychology, focused solutions therapies based on mindfulness, and leadership coaching to drive patients' self-empowerment mechanisms to various stages of learning and change[28]. For cancer patients, the health coaching process aims to mobilize the recognition and use of their own resources for self-management of symptoms and better outcomes.

In a controlled, blind, parallel-group, quasi-experimental pilot trial, a psychoeducation and coaching intervention performed by a nurse was associated with a significant reduction in symptom clustering severity, fatigue severity, fatigue interference, sleep disturbances, depression, and anxiety[29]. No significant differences were observed regarding pain severity, pain interference, functional status, and health-related quality of life. The effectiveness of a psychoeducational intervention was evaluated in a randomized trial in patients with lung cancer in the group of symptoms of anxiety, dyspnea, and fatigue[29]. Symptom management education and training in the use of progressive muscle relaxation resulted in a significant difference between the experimental group and the control group receiving usual care, in the pattern of change of symptom cluster, with significant effects on the pattern of changes in shortness of breath, fatigue, anxiety, and functional capacity[12].

Health coaching and cognitive behavioral therapy techniques have been used to reformulate pain, providing a sense of control and self-efficacy[30], as well as cognitive-behavioral interventions to change habits or perspectives, and breathing and relaxation practices interventions have been explored for symptom cluster management[30]. The positive impact of health coaching on pain management in cancer patients has been demonstrated in reviews and meta-analyses[26,30]. A comprehensive analysis of these data proposes that optimal strategies include patient-centered interventions tailored to individual needs, incorporated into therapeutic relationships and healthcare professional-patient communication, enabling patients to self-manage and coordinate their care in an integrated manner with standard cancer care. As the nurse is the one most directly involved in symptom management of cancer patients, the potential of training this professional to use health coaching processes in the promotion of self-care and self-efficacy in cancer patients is clear, and will contribute to symptom management and improved sickness behavior.

It should be noted that the present theoretical study articulated Psychoneuroimmunology with Middle Range Theories, methodologies and techniques that can also be explored in other interpretive contexts.

FINAL CONSIDERATIONS

Recent approaches to PNI have shown a vast field of analysis to understand the connections between different systems and bio-behavioral changes in patients in different contexts, particularly in the field of Oncology. Such connections should not be neglected or underestimated in biomedical research, as they may be responsible for phenomena that have not yet been fully elucidated. The integration of these complex connections of biological systems has become increasingly important and emergent for Oncology Nursing. Furthermore, therapeutic interventions whose targets are the neuroimmunoendocrine axis are promising for personalized nursing care, due to their ability to interfere in the physiology of biological systems and modulate the immune response directed to tumors, providing greater scientificity and autonomy in the care of clients by nurses. Ultimately, interventions promoting self-efficacy, such as health coaching, are tools that can be used by nurses to promote symptoms self-management by cancer patients.

RESUMO

Objetivo: Discutir a evolução das pesquisas em psiconeuroimunologia do câncer, os avanços no manejo dos *clusters* de sintomas neuropsicológicos e sua interface com teorias de médio alcance e aplicações práticas pela Enfermagem. **Método:** Estudo teórico-reflexivo ancorado em literatura recente, bem como na análise crítica dos autores. **Resultados:** Este é um campo promissor de investigação, que enfatiza a complexidade e a interação dos sintomas, as inter-relações entre os mesmos, os fatores que os influenciam e suas consequências. Subsidiadas por teorias de médio alcance em Enfermagem, como a Teoria dos Sintomas Desagradáveis e a Teoria de Gerenciamento de Sintomas, análises destas inter-relações corroboram os diagnósticos e as intervenções de Enfermagem em Oncologia. **Conclusão:** Propõe-se uma abordagem inovadora para qualificar o cuidado de Enfermagem Oncológica a partir da integração de avanços recentes em psiconeuroimunologia do câncer, teorias de médio alcance de Enfermagem, e ferramentas práticas como *coaching* de saúde. A abordagem proposta pode fortalecer a prática clínica da Enfermagem no manejo dos *clusters* de sintomas neuropsicológicos em oncologia e deve ser integrada na tomada de decisões durante o tratamento oncológico, favorecendo o cuidado centrado na pessoa.

DESCRITORES

Psiconeuroimunologia; Enfermagem Oncológica; Sintomas Concomitantes; Neuroimunomodulação; Neoplasias; Tutoria.

RESUMEN

Objetivo: Discutir la evolución de las investigaciones en psiconeuroinmunología del cáncer, los avances en el manejo de los *clusters* de síntomas neuropsicológicos y su interface con teorías de rango medio y aplicaciones prácticas por la Enfermería. **Método:** Estudio teórico-reflexivo ancorado en literatura reciente, así como en el análisis crítico de los autores. **Resultados:** Este es un campo promisor de investigación, que tiene énfasis en la complejidad y la interacción de los síntomas, las interrelaciones entre ellos, los factores que los influyen y sus consecuencias. Subsidiadas por teorías de rango medio en Enfermería, como la Teoría de los Síntomas Desagradables y la Teoría del Manejo de Síntomas, análisis de estas interrelaciones corroboran los diagnósticos y las intervenciones de Enfermería en Oncología. **Consideraciones Finales:** Se ha propuesto un abordaje innovador para calificar el cuidado de Enfermería Oncológica a partir de la integración de avances recientes en psiconeuroinmunología del cáncer, teorías de rango medio de Enfermería y herramientas prácticas como *coaching* de salud. El abordaje propuesto puede fortalecer la práctica clínica de Enfermería en la gestión de los *clusters* de síntomas neuropsicológicos en oncología y debe ser integrado en las acciones y decisiones durante el tratamiento oncológico que favorezcan el cuidado centrado en las personas.

DESCRIPTORES

Psiconeuroinmunología; Enfermería Oncológica; Síntomas Concomitantes; Neuroinmunomodulación; Neoplasias; Tutoría.

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