Editorial

Psychoneuroimmunology and Nursing research: discovery, paradigm shifts, and methodological innovations

The term "Psychoneuroimmunology" (PNI) has emerged in 1970 with the study by Robert Ader[1] and, since that, it has been promoted as an expression to designate the field of the science that study in an interdisciplinary manner the interaction between the psychological process and neural, endocrine, and immune function, as well as how such interaction influences health.

In last decade, a growing body of search involving neuroimmunomodulation has provided considerable evidences and new insights that support this emerging field of science, particularly for the variety of these physical stressors and spiritual psychosocial that can change the immune response via the psychoneuroimmunoendocrinology.[2]

According to framework of PNI, inflammatory mediators and others innate immune mediators can result in signaling to the central nervous system (CNS), stimulate the production of cytokines, change the neuronal, and trigger the "sickness behavior"- as an adaptative response.[2,3] The term sickness behavior was coined by Stephen Kent and collaborators in 1992[4] to mention a set of behavioral changes that follow a great number of pathological process occurring, apparently, without connection. Kent et al. also mentioned some modified behavior during diseases such as the occurrence of changes in standard of sleep and loss of interest by daily and positive activities, e.g., how to search for alignment, social contact, and sexual interest.[4]

Emerged the analysis infectious process of a number of origins, the history of sickness behavior was initially marked by the study of effects of bacterial products on the behavior. Among other bacterial products analyzed some of them were the LPS, and lipopolysaccharide of outer membrane of gram-negative bacteria.[5] After that, other pathological situations, for example, growth of neoplasia and autoimmune disease, which included a variety of processes that can generate a sickness behavior.[6]

Similarly to sickness behavior phenomena presented by laboratory animals, in humans, clinical picture including fatigue, pain, insomnia, depression, and cognitive disorders also were observed in patients with cancer, who show high levels of expression of pro-inflammatory cytokines.[2,6,7] The cause of sickness behavior picture in cancer patients contributed to the evolution of a new concept – the neuropsychological symptom clusters – that

is defined by a set of emotional symptoms or behavior that can be related to psychological or neurological dysfunction that has tendency to occur among cancer patients.[7]

There is a consciousness growth that common mechanisms can be underlined to the interaction between the nervous, endocrine and immune systems that regulate a set of responses capable of cause behavior and physiological changes in animals and humans.[6] Studies that cover sickness behavior, as well as neuropsychological symptom clusters in patients with cancer, support the hypothesis that pro-inflammatory cytokines are related to underlying biological mechanisms to the appearance of these symptomatology cluster .[2,6,7] The release of cytokines, such as IL-1β, IL-6, IL-8, IL-10, IL-12p70, TNF-α and IFN-y, for example, result in neuropsychological symptoms, including depressed humor, fatigue, depression, sleep disorders, and increase of pain sensibility. Changes in cytokines and other psychoneuroimmunology process can be critical to the symptoms onset and, potentially, to their prevention and treatment.[2,6,7] In this sense, the PNI supports the idea of the cascade of immune-cerebral communication can be related to the development of a number of diseases, as well as the appearance of unpleasant symptoms cluster relate to their treatment, measured by a number of inflammatory and neuroimmune-endocrine process.[2,6]

Researchers on the PNI conducted by nursing studies were relatively limited in the past. In Brazil, one of the first studies on the subject evaluated the effects of nursing-relaxing intervention in natural killer cells activity in women with breast cancer.[8] However, this research topic has become even more common particularly among nurses who complete academic degrees in basic sciences, and also among those who develop and integrate teams of researchers of basic areas, as well as those who became more conscience of projections related to PNI science.[9,10] The result of these collaborations is reflected on the synergic growth in translational investigation and interdisciplinary focused on fusion of biological, psychological and sociocultural dimensions of patient care, given the improvement of their health outcomes.[10]

Results of scientific investigation in basic science developed by nurses are based on personalized care. These investigations contribute with perception of complex interactions and variations that occur in biological system, that are intrinsically related to daily care provided to patients.[9,10] Unpleasant symptoms, such as pain, fatigue, anxiety, and changes in sleep patterns, among others, are reported daily in clinical practice to nursing professionals. Nurses should be encouraged to be involved with basic science in order to understand how clinical care and management can influence the discoveries conducted in the laboratory. Therefore, this is paramount that nurse to participate and identify strategies to speed up translational research considering a professional practice scenario with the aim to help the understanding of underlying psychopathological mechanism associated with these symptoms, aiming to intervene effectively.[10]

Nursing professionals are in an ideal position to develop personalized interventions, because, clearly, they are professionals who are in front line of care, and who provide continuous care to patients. In addition, nurses are asked to perform an integral care to the patient by adopting the best evidence available in the published literature, both to the neuropsychological symptom clusters management, as well as to engage in a continuous cycle the updating and new applications in clinical practice aiming to deliver a personalized intervention to the patient. It is important to consider the process of continuous education for nurse professionals in a way to training them on the new demands from the PNI, especially in new technologies and on available genomic information. This training should be done in order to help them to understand and interpret results of biomarker test related to efficacy from a variety of pharmacological and non-pharmacological intervention for neuropsychological symptom clusters and administration of therapies-target based on genetic constitution of each patient (pharmacogenomic).[10] However, there are always the need to consider holistic standard and patient and family center in such a way to integrate new knowledge to the nursing process.

These aspects reaffirm and support the evidence based practice (EBP) by considering the scientific autonomy provided by this professionals, given base to a safety clinical practice. However, both PNI and the PBE, are still occurring in a little segment in the Brazilian nursing universe. To encourage the development of searchers by nursing that has the goal to incorporate and implement the use of safety new practice and procedures with the goal on health prevent, promotion, and recovery. Applying discoveries and results from studies conducted by nurses may increase these professionals autonomy and provide scientific evidence to the care actions provided by nurses to patients and their family.

Studies on PNI area have the potential to validate care aspects of nurses who intuitively benefit patients, in addition, for example, in relation to the support of implementing complementary therapies in nursing practice along with scientific support.[11-14]

One of the main goals of the research of PNI is to determine the existence of one valid association between risk factors and immunological outcomes. If, at one hand, methods used in this type of research are not easily available for nursing investigators who generally are conducting studies with limited resources, on the other hand, nurses use a variety of parameters that consider the physiological changes within a complex psychosocial context. Therefore, studies to evaluate the value of nursing intervention, if projected with integral perspective on PNI, would allow the nurses to evaluate what such professionals affirm taking into consideration intuitively, as well as which biological and behavioral process are intimally correlated and need to be considered in term of care delivery to patients, in a way that will support with them in terms of quality and safety in their health-disease-care process journey.[9]

Currently, one of the main challenge topics for nurses, both in the research environmental or clinical practice, is the management of neuropsychological symptom cluster related to a number of diseases.[2,15] In general, studies in oncology are, in most of the cases, concentrated in study of prevalence and treatment of isolated symptoms, contrary to consider them agglomerated. However, we know in clinical practice, the symptoms are rarely occurring separately. They can be clustered, creating the synergy effect that lead to an increase of intensity or an antecessor effect that can predict the development of future symptoms.[2,7,15]

Nursing researchers must be aware and sensitized about the experience of patients in relation to these unpleasant symptoms. The study of these factors may generate great opportunity of the research, such as, for example: a) trajectory, development and severity of these symptoms throughout the time (treatment and post-treatment) ; b) inter-relations between these symptoms by age range, by sociocultural and spiritual aspects, by diagnosis and by treatment phase; c) as occur in formation of grouping among them. There are great potential to advance nursing by studies that evaluate psyco-neuroimmunoendrocrine pathways involved in genesis of these symptom clusters.

Such studies would provide a basis for development of future intervention. We highlight the management of these symptoms, and this is important question and vital aspect of nursing practice, given their important role performed in clinical assessment, in monitoring of symptoms and their therapeutic collateral effects. Until the most defined studies of symptom clusters would be conducted, nurses need to follow-up patients for co-occurrence of multiple symptoms and develop plans of personalized care, using the PNI in agreement with care to overcome PBE.

Due to the apparent linking between these symptoms and biological mechanisms, studies that are designated to improve the possible bimolecular mechanisms constitute an important area of study. In this nursing context, research that guarantee the best understanding about the etiology and psychosocial mechanisms of unpleasant symptom clusters which will allow the nursing intervention that would be proposed with scientific support. Once identified the association or sensibility degree and specificity of biomarkers, they would be used in response to nursing intervention in order to enable to determine with accuracy their efficacy. In other words, to whom and what context these intervention will work (what dose, type, frequency), when they would be employed (before, during or after the treatment), and how long time (duration).[10,16]

Recent approach to PNI has shown a large analyses field to understand connections among systems and biobehavioral changes in patients in different contexts. Such connections must be forgot or underestimated in any biomedical research, because they can be responsible for phenomenon that is still little understood. The integration of biological and psychological model have become even more important in health-disease-process. In addition, therapeutic intervention that targe neuroimmunoendrocrine axis are

promising for personalized care in health, because this may turn possible the ability to interfere in nervous physiological systems and endocrine and modular to immune response.

To understand how this neuroimunendocrine pathways regulate the development of the disease, as well as underlying aspects to specific therapeutic, such as immunotherapy, constitute an important frontier for future investigation. Such understand can contribute to elucidate the diagnosis and prognosis of a number of diseases and as well as how the support in the selection of personalized therapies is more suitable for each patient or for each type of disease. Finally, we highlight that PNI field involves, in addition to the scientific issues, financial, ethical, and legislative subjects, as well as regulators and operations, which transport how important challenges for these translational researchers are, in order to optimize, became viable and well-succeeded to the translational research process. Despite this area of study constitutes a challenge for nursing, the field of translation can provide benefits for individual and their families, particularly as a powerful promising tool to improve their quality of life.

Maria Helena Costa Amorim
Visiting Full Professor at Paulista Nursing School, Federal University of São Paulo, São Paulo, SP, Brazil.
https://orcid.org/0000-0002-4252-7092

Luís Carlos Lopes-Júnior
Assistant Professor of the Nursing Department, Federal University of Espírito Santo, Vitória, ES, Brazil.
https://orcid.org/0000-0002-2424-6510

How to cite:
Amorim MH, Lopes-Júnior LC. Psychoneuroimmunology and Nursing research: discovery, paradigm shifts, and methodological innovations. Acta Paul Enferm. 2021;34:e-EDT1.**DOI:** http://dx.doi.org/10.37689/acta-ape/2021EDT1.

References

1. Ader R. On the development of psychoneuroimmunology. Eur J Pharmacol. 2000;405(1-3):167–76.
2. McDonald GP, O'Connell M, Lutgendorf SK. Psychoneuroimmunology and cancer: a decade of discovery, paradigm shifts, and methodological innovations. Brain Behav Immun. 2013;30 Suppl:S1-9.
3. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. Nat Rev Neurosci. 2008;9(1):46–56.

4. Kent S, Bluthé RM, Kelley KW, Dantzer R. Sickness behavior as a new target for drug development. Trends Pharmacol Sci. 1992;13(1):24–8.

5. Renault J, Gheusi G, Aubert A. Changes in social exploration of a lipopolysaccharides-treated conspecific in mice: role of environmental cues. Brain Behav Immun. 2008;22(8):1201–7.

6. Dantzer R, Kelley KW. Twenty years of research on cytokine-induced sickness behavior. Brain Behav Immun. 2007;21(2):153–60.

7. Kim HJ, Barsevick AM, Fang CY, Miaskowski C. Common biological pathways underlying the psychoneurological symptom cluster in cancer patients. Cancer Nurs. 2012;35(6):E1–20.

8. Amorim MH, Rumjanek V. O efeito da intervenção de Enfermagem relaxamento nas células com atividade natural killer em mulheres com câncer de mama. In: VI Colóquio Pan-Americano de Investigação em Enfermagem. Anais... Ribeirão Preto: 1998; p.344.

9. Langley P, Fonseca J, Iphofen R. Psychoneuroimmunology and health from a nursing perspective. Br J Nurs. 2006;15(20):1126–9.

10. Lopes-Júnior LC, Olson K, de Omena Bomfim E, Pereira-da-Silva G, Nascimento LC, de Lima RA. Translational research and symptom management in oncology nursing. Br J Nurs. 2016;25(10):S12, S14, S16 passim.

11. Primo CC, Amorim MH, Leite FM. A intervenção de Enfermagem-Relaxamento e seus efeitos no sistema imunológico de puérperas. Acta Paul Enferm. 2011;24(6):751–5.

12. Silva HL, Almeida MV, Diniz JS, Leite FM, Moura MA, Bringuente ME, et al. Efeitos da auriculoterapia na ansiedade de gestantes no pré-natal de baixo risco. Acta Paul Enferm 2020;33:eAPE20190016.

13. Olympio PC, Lima E, Amorim MHC. Mulher mastectomizada: Intervenções de Enfermagem e atividade natural killer. Rev Epidemiol Control Infect. 2014;4(1):7-11.

14. Araújo WS, Romero WG, Zandonade E, Amorim MH. Effects of relaxation on depression levels in women with high-risk pregnancies: a randomised clinical trial. Rev Lat Am Enfermagem. 2016;24(0):e2806.

15. Dodd MJ, Miaskowski C, Lee KA. Occurrence of symptom clusters. J Natl Cancer Inst Monogr. 2004;2004(32):76–8.

16. Berger AM, Yennu S, Million R. Update on interventions focused on symptom clusters: what has been tried and what have we learned? Curr Opin Support Palliat Care. 2013;7(1):60–6.