AGE-DEPENDENT STRUCTURAL AND INFLAMMATORY RESPONSES OF THE CECUM TO SLEEP DEPRIVATION AND THEIR PHYTOCORRECTION

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Abstract

Sleep deprivation is increasingly regarded as an important systemic stress factor that can affect not only the nervous system but also the structure and function of peripheral organs. The gastrointestinal tract is particularly sensitive to disturbances in neuroendocrine and immune regulation because intestinal tissues are continuously exposed to systemic stress mediators and contain extensive components of the local immune system. Although the relationship between sleep disturbances and gastrointestinal function has received increasing attention, age-related changes in the response of the large intestine, especially the cecum, to prolonged sleep deprivation remain insufficiently studied.

This thesis examines age-related differences in the structural and inflammatory response of the cecum to experimental sleep deprivation and assesses the potential protective effects of selected plant-derived preparations. The experimental study is performed on white laboratory rats from three age groups: 3, 9, and 15 months. The inclusion of these age groups allows comparison of the response of the cecal wall at different stages of postnatal development and aging and makes it possible to determine whether susceptibility to prolonged sleep deprivation changes with age.

Morphological assessment is focused on the main layers of the cecal wall, including the mucosa, submucosa, and muscular layer. Particular attention is paid to the height of the surface epithelium, crypt depth, and the quantitative characteristics of lymphoid structures involved in intestinal immune defense. Changes in these parameters are evaluated as indicators of structural remodeling and adaptation of the cecal wall under prolonged physiological stress.

The inflammatory response is assessed immunohistochemically by determining the expression of NLRP3 inflammasome-related markers in the cecal tissue. NLRP3 is an important component of innate immune signaling and is involved in inflammatory responses triggered by cellular and tissue stress. Its expression in the cecal wall therefore provides additional information about local inflammatory activation and complements the results obtained from histomorphometric examination.

The study also evaluates the corrective effects of rosemary and ginseng extracts administered separately and in combination. Their effectiveness is assessed by comparing changes in the structural parameters of the cecal wall together with alterations in NLRP3 expression. Particular attention is given to the combined administration of the two preparations, as their biological properties may have complementary protective effects under conditions of prolonged sleep deprivation.

Another objective is to determine whether the association between structural changes and inflammatory activity differs among the studied age groups. For this purpose, correlation analysis is used to examine relationships between selected morphometric parameters and immunohistochemical findings. This makes it possible to assess morphological and inflammatory

changes as interconnected components of the tissue response rather than as separate phenomena.

The study is expected to demonstrate that the response of the cecal wall to prolonged sleep deprivation differs depending on the age of the animals. These differences may be reflected in changes in epithelial height and crypt depth, alterations in lymphoid structures, and variation in the intensity of NLRP3 expression. Comparative assessment of rosemary, ginseng, and their combined administration may also reveal differences in their ability to reduce or prevent structural and inflammatory changes associated with sleep deprivation.

The significance of the research lies in the combined assessment of age-related factors, tissue morphology, local inflammatory activity, and phytocorrection within a single experimental model. The results may contribute to a better understanding of the mechanisms underlying sleep-deprivation-induced changes in the intestinal wall and provide a basis for further experimental studies of plant-derived preparations as potential approaches for preventing or correcting stress-related gastrointestinal alterations.

Keywords: sleep deprivation, cecum, cecal wall, age-related changes, histomorphometry, immunohistochemistry, NLRP3 inflammasome, intestinal epithelium, crypts, GALT, lymphoid follicles, rosemary, ginseng, phytocorrection, gastrointestinal stress response.

INTRODUCTION

Sleep is an essential biological process involved in the regulation of neural, endocrine, metabolic, and immune functions. Although the consequences of inadequate sleep are most commonly discussed in relation to

the central nervous system, prolonged disruption of normal sleep patterns can produce systemic effects involving multiple organs and physiological systems.

The gastrointestinal tract represents an important target of these systemic effects. Communication between the nervous, endocrine, immune, and intestinal systems is mediated through complex regulatory pathways, and disturbances in one component of this network may influence the others. Experimental and clinical observations indicate that persistent sleep disturbance may be associated with changes in intestinal motility, epithelial homeostasis, immune regulation, and inflammatory signaling.

The cecum occupies a specific position within the large intestine and performs important digestive and immunological functions. Its wall contains a highly organized mucosal surface, intestinal crypts, connective tissue components, muscular structures, and lymphoid formations associated with gut-associated lymphoid tissue. Consequently, morphological changes in the cecum may reflect both local tissue adaptation and systemic disturbances in immune and stress regulation.

An important unresolved issue is whether the response of the cecal wall to sleep deprivation is dependent on age. The structural organization and functional capacity of intestinal tissues change throughout the lifespan. At different ages, epithelial renewal, immune responsiveness, tissue repair, and inflammatory regulation may differ substantially. Therefore, an identical stressor may produce different morphological and immunological consequences in young, mature, and older animals.

The NLRP3 inflammasome is of particular interest in this context. As a component of innate immune signaling, NLRP3 participates in the recognition and response to cellular stress and has been implicated in inflammatory processes in various tissues. Evaluation of NLRP3 expression in the cecal wall

may therefore provide additional information about the local inflammatory response accompanying sleep deprivation.

At the same time, the search for approaches capable of reducing stress-induced tissue alterations has increased interest in biologically active plant preparations. Rosemary and ginseng contain a range of biologically active compounds and have been investigated for antioxidant, anti-inflammatory, and adaptogenic properties. However, their potential influence on age-dependent morphological and immunohistochemical changes in the cecum under conditions of sleep deprivation requires further experimental investigation.

AIM OF THE STUDY

The aim of the study is to determine the age-dependent morphological and immunohistochemical response of the cecal wall to experimental sleep deprivation and to evaluate the comparative effectiveness of rosemary and ginseng extracts, administered separately and in combination, in attenuating the associated structural and inflammatory alterations.

OBJECTIVES OF THE STUDY

To achieve this aim, the following objectives are established:

1. To characterize the normal histomorphometric organization of the cecal wall in 3-, 9-, and 15-month-old rats.
2. To determine age-related differences in the thickness and structural organization of the mucosal, submucosal, and muscular layers of the cecum.
3. To assess changes in epithelial height and intestinal crypt depth associated with experimental sleep deprivation.

4. To quantify changes in the number and area of lymphoid follicles representing an important component of the local intestinal immune system.

5. To determine the expression of NLRP3 inflammasome in the cecal wall under normal conditions and following sleep deprivation.

6. To compare the intensity of morphological and immunohistochemical changes between different age groups exposed to the same experimental stress.

7. To evaluate the effects of rosemary extract on sleep-deprivation-associated alterations in cecal morphology and NLRP3 expression.

MATERIALS AND METHODS

The experimental study is performed on white laboratory rats divided according to age into three groups: 3-month-old, 9-month-old, and 15-month-old animals. Within each age category, animals are distributed among control, sleep-deprivation, and corrective-treatment groups.

An experimental model of sleep deprivation is established under controlled laboratory conditions. The experimental protocol is designed to reproduce sustained disruption of normal sleep while maintaining standardized environmental conditions for all animals.

For the corrective intervention, rosemary extract and ginseng extract are administered separately to designated experimental groups. An additional group receives a combination of both preparations. The control animals are maintained under standard conditions without sleep deprivation or phytocorrection.

Following completion of the experimental period, cecal tissue specimens are collected for histological and immunohistochemical examination.

EXPECTED RESULTS

The study is expected to establish clear age-related differences in the structural organization of the cecal wall under physiological conditions.

Sleep deprivation is expected to produce measurable changes in the mucosa, crypt architecture, epithelial characteristics, and lymphoid structures. The magnitude and direction of these changes may vary between young, mature, and older animals, reflecting differences in tissue adaptation and regenerative capacity.

An increase in NLRP3 expression is expected to accompany the structural alterations associated with sleep deprivation. The degree of NLRP3 activation may differ between age groups, providing evidence that age influences the inflammatory response of the intestinal wall to prolonged sleep disturbance.

The administration of rosemary and ginseng is expected to reduce some of the morphological and immunohistochemical abnormalities associated with sleep deprivation. However, the two preparations may demonstrate different patterns of effectiveness. Comparative analysis of individual and combined administration will make it possible to determine whether the combination provides additional protective effects.

Correlation analysis is expected to clarify whether increased NLRP3 expression is associated with specific morphological changes, including alterations in epithelial height, crypt depth, mucosal thickness, and lymphoid follicle characteristics.

SCIENTIFIC NOVELTY

The scientific novelty of the study lies in the comprehensive assessment of age-related structural and inflammatory changes in the cecum under conditions of prolonged sleep deprivation. The study considers morphological alterations of the cecal wall together with changes in local immune activity, with particular attention to NLRP3 expression.

Unlike studies that focus mainly on either intestinal morphology or inflammatory responses to sleep deprivation, the present investigation considers several related aspects within a single experimental model. These include age-related differences in the response of the cecal wall, quantitative changes in its structural parameters, alterations in GALT-associated lymphoid structures, and changes in NLRP3 expression. The relationships between selected morphometric and immunohistochemical parameters are also examined to provide a more complete characterization of the tissue response.

Another aspect of the study is the comparative assessment of rosemary and ginseng extracts administered separately and in combination. This approach makes it possible to evaluate their potential effects on sleep-deprivation-associated structural and inflammatory changes and to determine whether combined phytocorrection produces a different response from the use of each preparation alone.

PRACTICAL SIGNIFICANCE

The results of the study may be useful for experimental morphology, histology, immunology, and physiology by providing quantitative information about age-related changes in the cecum under conditions of prolonged sleep disturbance.

The identified morphological and immunohistochemical indicators may also be considered potential experimental markers for assessing the severity of intestinal alterations associated with chronic sleep deprivation.

The comparative findings concerning rosemary and ginseng may serve as a basis for further experimental research into phytocorrective strategies aimed at reducing tissue damage and inflammatory activation associated with prolonged physiological stress.

CONCLUSION

Sleep deprivation should be viewed not simply as a disruption of the normal sleep–wake cycle, but also as a systemic stress condition that can influence the structure and immune function of peripheral organs. The cecum is of particular interest in this regard because of its distinct epithelial organization and well-developed lymphoid tissue, which make it suitable for studying structural and immune changes associated with prolonged stress.

In this study, particular attention is given to age-related differences in the response of the cecal wall to prolonged sleep deprivation. Animals from different age groups are examined to determine whether the extent of structural changes varies with age. Histomorphometric examination is combined with immunohistochemical assessment of NLRP3 expression, allowing morphological alterations to be considered alongside changes in local inflammatory activity.

The assessment of NLRP3 expression is intended to provide further information about the involvement of innate immune mechanisms in the response of cecal tissue to sleep deprivation. The study also compares the effects of rosemary and ginseng extracts administered separately and in combination. This comparison makes it possible to assess whether these plant-derived preparations can reduce the structural and inflammatory

changes associated with prolonged sleep deprivation and whether their combined use produces a more pronounced effect.

Taken together, the findings are expected to clarify age-related differences in the response of the cecal wall to sleep deprivation and to indicate whether phytocorrection can influence both morphological and inflammatory changes. The results may contribute to a better understanding of the relationship between prolonged sleep disturbance, intestinal tissue remodeling, and local immune responses.