BACTERIAL NEUROLOGICAL DISEASES INFLUENCED BY GLOBAL WARMING

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Introduction. *In recent years, the incidence of infectious diseases affecting the central nervous system has increased. Among the reasons for the expansion of these diseases and the emergence of new neuropathogens are globalization, global warming, increased proximity between humans and wild animals due to human activities such as deforestation, the rising cases of antimicrobial resistance, etc.*

Material and methods. *A narrative synthesis of specialized bibliographic references was conducted, selecting sources from Google Scholar and ResearchGate using the keywords "bacterial diseases of the nervous system," "neuroinfections," and "global warming" in English. A total of 39 bibliographic sources were identified, excluding 3 abstracts and 4 duplicated articles. Additionally, 19 irrelevant articles were excluded, and 4 articles highlighting the topicality of the subject were added.*

Results. *Bacterial diseases affecting the nervous system tend to become increasingly severe due to the critical functions performed by the brain, spinal cord, peripheral nerves, and cranial nerves. Infections can occur in nervous tissue or in the meninges (covering membranes). Specialized literature mentions that there is no direct connection between neuroinfections and global warming. The development of neuroinfections is linked to exposure to bacterial agents in the environment and is associated with human behaviors. Although global warming can influence the distribution of disease vectors, there is a significant distance between this phenomenon and the direct transmission of neuroinfections. Global warming can impact human health in various ways, including the expansion of the range of vector-borne diseases or changes in the distribution of pathogens. However, these connections are complex and depend on numerous factors.*

Conclusions. *The effects of global warming can enhance the adverse impact of microorganisms on the nervous system.*

Cuvinte-cheie: *sistem nervos central, maladii bacteriene, neuroinfecții.*

MALADII BACTERIENE NEUROLOGICE INFLUENȚATE DE ÎNCĂLZIREA GLOBALĂ

Introducere. *În ultimii ani a crescut incidența bolilor infecțioase care afectează sistemul nervos central. Printre motivele expansiunii acestor boli și apariției de noi neuropatogeni se numără globalizarea, încălzirea globală, apropierea crescută dintre oameni și animalele sălbatice din cauza activităților umane precum defrișările, creșterea cazurilor de rezistență antimicrobiană etc.*

Material și metode. *A fost realizată o sinteză narativă a referințelor bibliografice de specialitate. Sursele au fost selectate în Google Scholar și ResearchGate folosind cuvintele-cheie „maladii bacteriene ale sistemului nervos", „neuroinfecții" și „încălzire globală" în limba engleză. Astfel au fost identificate 39 de surse bibliografice, dintre care au fost excluse trei abstracte, patru articole dublate, 19 articole netematice și au fost adăugate patru articole ce reflectă actualitatea temei.*

Rezultate. *Bolile bacteriene, care afectează sistemul nervos, au tendință de a deveni tot mai grave din cauza funcțiilor critice pe care le îndeplinesc creierul, măduva spinării, nervii periferici și cranieni. Infecțiile pot apărea în țesutul nervos sau în meninge (membranele de acoperire ale creierului). În literatura de specialitate se menționează că nu există o conexiune directă între neuroinfecții și încălzirea globală. Dezvoltarea neuroinfecțiilor are legătură cu expunerea la agenții bacterieni din mediu și cu comportamentele umane. Deși încălzirea globală poate influența distribuția unor vectori ai bolilor, există o distanță semnificativă între acest fenomen și transmiterea directă a neuroinfecțiilor. Încălzirea globală poate afecta sănătatea umană într-o varietate de moduri, inclusiv prin extinderea ariei de răspândire a unor boli transmise de vectori sau prin schimbări în distribuția unor agenți patogeni, dar aceste legături sunt complexe și depind de numeroși factori.*

Concluzii. *Efectele încălzirii globale potențează acțiunea nefavorabilă a microorganismelor asupra sistemului nervos.*

INTRODUCTION

The progress in human health and diseases has been substantial in today's world, with a growing emphasis on exploring the causal relationships between various illnesses and diverse causative factors, both internal and external. There is limited conclusive data or few pieces of evidence to suggest that climate change/global warming is responsible for altering disease patterns. However, extreme temperature fluctuations, such as heatwaves and cold spells, coupled with changes in precipitation levels leading to famine and floods, and the presence of airborne allergens with increased air pollution, impact human health at an individual level. Vector-borne diseases are directly affected by changes in temperature and precipitation levels. Water-related diseases arising from poor water quality, its quantity, and insufficient personal hygiene have complex associations. The loss of human lives, damage to health infrastructure, and public properties due to recent disasters like storms, cyclones, and hurricanes serve as a warning for the future world to address this situation now or never. On the other hand, the vulnerable population in low- or middle-income countries bears the brunt of the health burden related to global warming (1). Together, these factors will have adverse consequences on the health status of the population, including the health of the human brain (2).

Neurotropism, which affects the normal function of the brain, is characteristic of certain microorganisms such as prions, viruses, bacteria, fungi, and parasites (3). Bacterial infections of the central nervous system are significant causes of morbidity and mortality. Neuroinfections caused by these agents activate the immune response, inducing neuroinflammation, excitotoxicity, and neurodegeneration. Purinergic signaling is an evolutionarily conserved signaling pathway associated with these neuropathologies (4).

Global warming is a phenomenon of great concern, given the increasing temperature and frequency of extreme weather conditions directly impacting all life on Earth. The planet's temperature is rising at an unprecedented rate, leading to the loss of biodiversity. Biodiversity is a term that encompasses both macro and microenvironments. Altered biodiversity, the duration of pollination seasons and geography, coupled with the production of harmful gases, released toxic substances, and chemicals, underscore the rise in disturbances related to the epithelial barrier (5, 6).

The incidence of infectious diseases affecting the central nervous system (CNS) has increased in recent years. Among the reasons for the expansion of these diseases and the emergence of new neuropathogens are globalization, global warming, and increased proximity between humans and wild animals due to human activities such as deforestation (4).

The anatomy of the brain and meninges determines the unique nature of infections of the central nervous system, often referred to as neuroinfections.

Many inflammatory conditions have been influenced by a disrupted epithelial barrier, best explained by the hypothesis of the epithelial barrier (6).

The increasingly frequent extreme weather events can synergistically damage the integrity of the epithelial barrier. A compromised epithelial barrier induces pro-inflammatory activation of epithelial cells. An "open" epithelial barrier contributes to the entry of the external exposome into and beneath the epithelium, triggering an expulsion response led by local inflammatory cells and chronic inflammation. These changes are associated with microbial dysbiosis with opportunistic pathogenic colonizers and decreased commensal presence. These cellular and molecular events are key mechanisms in the pathogenesis of numerous chronic inflammatory disorders (5, 7).

Thus, mitigating the impact on health should be tailored to regional health threats. Effective strategies need to be devised at all levels of the healthcare delivery system (1, 2).

The *aim* of the research was to analyze the issues related to bacterial diseases of the CNS in association with global warming.

MATERIAL AND METHODS

The research represents a narrative synthesis of specialized bibliographic references from both domestic and international sources. The synthesis relied on the theoretical evaluation of scholars' experiences regarding the addressed phenomenon. Sources were selected through the *Google Scholar* search engine and the *ResearchGate* social

network. The keywords "bacterial diseases of the nervous system," "neuroinfections," and "global warming" were used in English. The primary criterion for selecting bibliographic sources was the availability of full, free access to the articles.

The first stage of the work included selecting articles that contain two components of interest in the research: bacterial diseases of the nervous system and global warming. At this stage, 39 bibliographic sources were identified on *Google Scholar* and *ResearchGate*. In the *second stage*, 3 abstracts and 4 duplicated articles were excluded. After a detailed analysis of titles and abstracts (*third stage*), articles containing relevant information for the research topic with both requested components were selected. Thus, the final number for analysis consisted of 12 scientific articles, supplemented with 4 articles used in the introduction = 16 scientific articles (fig. 1).

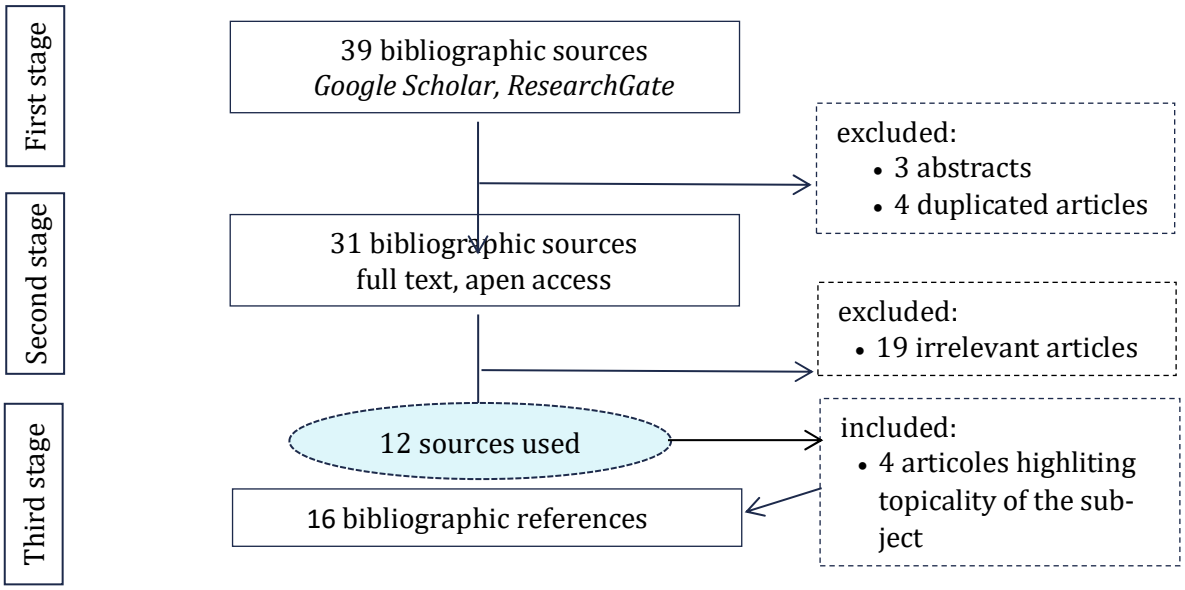

Figure 1. Article selection algorithm.

RESULTS

Bacterial diseases of the nervous system are very rare but can be life-threatening.

Microbiology of the nervous system

Bacterial diseases of the CNS continue to increase in incidence due to conditions contributing to the emergence of pathogens, such as global travel, climate changes, and human encroachment into animal territories. The severity and complexity of these diseases are influenced by the diversity of etiological agents and their routes of neuroinvasion (8).

Among the bacterial diseases affecting the nervous system are: meningococcal meningitis, pneumococcal meningitis, listeriosis, Lyme disease, tuberculoid leprosy, lepromatous leprosy, tetanus, botulism, etc. (4, 9). Epidural abscesses remain localized, while subdural abscesses spread over one of the cerebral hemispheres. Infections in the subarachnoid space tend to spread over the brain and spinal cord (8, 10).

The major bacterial causes of central nervous system infections are *Haemophilus influenzae, Streptococcus pneumoniae*, and *Neisseria meningitidis* (9). Most of these agents invade through the bloodstream. In these infections, the number of bacteria rapidly increases in the cerebrospinal fluid. Brain abscesses often present a mixed flora of aerobic and anaerobic bacteria (4).

The bacterial world and global warming

Microorganisms provide long- and short-term feedback reactions to global warming and climate changes, which can be both positive and negative. Since they can recycle and modify fundamental elements such as carbon and nitrogen that make up cells, they play a significant role as producers or consumers of these gases in the environment. In unpopulated areas that were previously too cold for bacteria to survive, they have been able to spread and can cause fatal infections (11).

New infections could arise as the gap between ambient temperatures and human body temperature narrows. Floods and other natural disasters are more likely, driven by climate changes, leading to an increased risk of bacterial growth in people's homes. In this context, certain bacteria can lead to severe contamination of the lungs and brain (11).

The capacity of the medical system to treat bacterial diseases is compromised by antimicrobial resistance (a threat in which microorganisms, especially bacteria, become resistant to antibiotics and disinfectants, thereby complicating the ability to treat and prevent infections). Resistance is often developed through sub-inhibitory exposures to drugs and/or disinfectants but can also be caused by (often negative) environmental changes as a response mechanism to environmental conditions such as air temperature, water salinity, metals (potential toxic elements), and organic pollutants. Possible mechanisms through which climate change could affect the transfer of antimicrobial resistance genes between bacteria include:

- direct action, through changes in air temperature and/or precipitation,
- indirect impact, such as changes in human populations, disease vectors, agricultural processes, water availability, glacial and hydrological processes (1).

The impact of global warming on neurological diseases

Exposure to heat can lead to hyperthermia and heatstroke in extreme cases, which can be fatal. As global temperatures continue to rise, the incidence of hyperthermia and heatstroke is also inevitably expected to increase. Hyperthermia, along with atmospheric changes associated with global warming, is linked to an increased prevalence of migraines, seizures, stroke, and certain forms of dementia, including Alzheimer's disease. Prolonged exposure to heat can elevate levels of proinflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1), and may induce gliosis and a decrease in synaptic density in the brain (2).

With global warming and the extremely hot summers witnessed worldwide in recent years, there is an increase in the incidence of fatal encephalitis caused by the so-called "brain-eating amoebas." (12).

The major cause of global warming is greenhouse gases that trap the thermal energy reflected by the Earth's surface. The main greenhouse gases include carbon dioxide, methane, nitrous oxide, and ozone. A new bacterium called *Methylokorus infernorum* has been discovered, which could help address the greenhouse gas issue. Found in geothermal areas with acidic and hot conditions, this bacterium utilizes methane gas. These bacteria can consume vast amounts of methane, approximately 11 kg/year, and could be useful in reducing ethane emissions from methane-producing facilities and landfills (13).

Bacteria can be involved in stopping global warming

Global warming has direct and indirect opposing effects on the structure and function of the microbial community in permafrost lake sediments.

Northern lakes disproportionately influence the global carbon cycle and may do so even more in the future, depending on how their microbial communities respond to global warming. Microbial communities can change due to the direct effects of global warming on their metabolism and the indirect effects of global warming on the connectivity of groundwater from permafrost thaw in the surrounding area (2).

Bacteria play a crucial role in the global carbon, nitrogen, and methane cycles. They capture carbon from non-living sources, making it available for living organisms through the process of carbon fixation. Bacteria can cycle carbon molecules under anaerobic conditions to produce energy through the fermentation process. Certain bacteria, such as *Thiobacillus ferrooxidans*, sulfur bacteria, and *Clostridium butyricum*, may participate in the carbon cycle (which describes the continuous movement of carbon atoms from the atmosphere to Earth and back to the atmosphere) (11, 14).

The main component of air, gaseous nitrogen (N_2), enters the biosphere through biological fixation. Bacteria exhibit specificity to certain plants. As a result of attaching to one of the plant's root hairs, the bacterium creates a hollow tube that leads into the root. Through this tube, bacteria develop and eventually form a nodule on the root. For bacteria, the plant provides food and energy, while nitrogen from the air is supplied in a form usable by the plant through fixation by the bacteria. *Rhizobium trifolium* contains the nitrogenase

enzyme, which fixes atmospheric nitrogen into a form of ammonium ions that is chemically advantageous for higher species. The plant transforms the fixed ammonium ion into nitrogen oxides and amino acids to create proteins and other compounds like alkaloids, as part of their symbiotic association. Bacteria contribute to the collection of energy or the accumulation of nitrogen in a form necessary for their growth and development. Bacteria that consume methane (CH_4), a greenhouse gas, are imperative for maintaining Earth's climate stability. Methane serves as an energy source for bacteria metabolism (11).

DISCUSSIONS

Neuroinfections begin nonspecifically, without signs of involvement of the nervous system.

Bacterial diseases affecting the nervous system tend to become more severe due to the critical functions performed by the brain, spinal cord, peripheral nerves, and cranial nerves. Infections can occur in nervous tissue or in the meninges (covering membranes).

Climate change is a global existential challenge that has introduced unprecedented pressures on the planet, already translating into significant consequences for human health.

The study conducted in Canada, sampling 19 lakes along a 1600 km latitudinal transect covering all major permafrost regions, assessed the potential impacts of global warming through spatial substitution over time. The direct effects of regional warming, such as temperatures and permafrost coverage extent, were compared with its indirect impacts on local groundwater connectivity and lake water chemistry. It was found that methanogens and metabolically diverse Euryarchaeota genes involved in all major pathways of methanogenesis responded particularly positively to the direct effects of regional global warming (15).

Some authors mention that increases in sequences representing methanogens and methanogenesis could be partially compensated by greater groundwater connectivity associated with warmer temperatures, as the abundance of these sequences has been negatively correlated with groundwater connectivity (16).

The opposing views among scientists on different aspects of global warming help explain why considerable variation remains unexplained in methane emission predictions by Earth system models, even when microbial dynamics are considered. The potential methane production can be further enhanced in warmer locations due to the inadequate increase in its oxidation.

The specialized literature mentions that there is no direct connection between neuroinfections and global warming. The development of neuroinfections is linked to exposure to bacterial agents in the environment and is associated with human behavior. Although global warming can influence the distribution of disease vectors, there is a significant distance between this phenomenon and the direct transmission of neuroinfections. Global warming can impact human health in various ways, including expanding the range of vector-borne diseases or altering the distribution of pathogens, but these connections are complex and depend on numerous factors (6, 17).

Nevertheless, it is important to understand and address the consequences of global warming on human health, including potential public health risks and possible impacts on the distribution of infectious diseases. Studies in this field are ongoing to investigate these connections and to develop effective adaptation and mitigation strategies.

The increase in methanogenesis is supported by concurrent measurements of methane fluxes at the study sites. Together, the results provide a new understanding of why methane emissions are highly sensitive to rising temperatures in the study region. Future predictions of methane emissions could now be improved by considering how microbial dynamics vary with the direct and indirect effects of global warming associated with temperature and hydrology (14).
Environmental changes can create additional stress on microorganisms and the distribution of pathogens. Further research is needed to understand the microbiome, resistance, and environmental stress factors (such as temperature) that modify the impact, wastewater treatment, pathogens discharged into the environment, and the evolution and dissemination after exposure to ecological stress (1).

Diagnostic tests for neurological disorders often involve examining cerebrospinal fluid, and antibiotic therapy must use medications that can cross the blood-brain barrier.

CONCLUSIONS

1. Climate change represents a shift in balance, and the outcomes of the interaction between environmental factors and bacteria, the connections between these components, are complex and challenging to predict.
2. The effects of global warming enhance the unfavorable action of microorganisms on the nervous system.

CONFLICT OF INTEREST

Authors have no conflict of interest to declare.

ETHICAL APPROVAL

As the article does not involve ethical risks, approval from the Ethics Committee was not deemed necessary for the research.

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