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REVIEW ARTICLE

Temperature-related climate change impacts on neurodegenerative diseases: systematic review

Impactos das mudanças climáticas relacionadas à temperatura nas doenças neurodegenerativas: revisão sistemática

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Abstract

Objective: Neurodegenerative diseases have been increasing in incidence, and it is interesting to monitor the possible relationship with environmental conditions. **Methods**: This Systematic Review aims to elucidate these associations through comprehensive searches of databases, such as PubMed Central, Medline, Cochrane Library, LILACS, Scopus, LIVIVO, Web of Science, and Embase, in addition to grey literature. **Results**: From 965 papers initially identified, eight met the eligibility criteria and were evaluated for risk of bias using Cochrane's ROBINS-E tool. Despite methodological diversity among the studies, the collective evidence indicates that exposure to extreme temperature events, particularly heat waves, may aggravate clinical outcomes in individuals with neurodegenerative diseases. The mechanisms proposed, though not yet fully characterized, include enhanced oxidative stress and neuroinflammation and, in the context of cold exposure, alterations in Tau protein phosphorylation. **Conclusions**: These findings emphasize the sensitivity of the nervous system to environmental stressors and suggest the necessity for further robust, longitudinal research to clarify causal pathways. Moreover, these signal the need for integrated public health strategies in order to mitigate the neurological impacts of climate change and protect vulnerable populations.

Keywords: neurodegenerative diseases; climate change; extreme weather; climate effects; systematic review

Resumo

Objetivo: doenças neurodegenerativas têm apresentado aumento em incidência, sendo interessante observar possíveis relações com fatores ambientais. **Métodos**: Esta revisão sistemática tem como objetivo elucidar essas associações por meio da busca em bases de dados como PubMed Central, Medline, Cochrane Library, LILACS, Scopus, LIVIVO, Web of Science e Embase, além da literatura cinzenta. **Resultados**: Dos 965 artigos inicialmente identificados, oito atenderam aos critérios de elegibilidade e foram avaliados quanto ao risco de viés usando a ROBINS-E tool da Cochrane. Apesar da diversidade metodológica entre os estudos, as evidências indicam que a exposição a eventos de temperaturas extremas, particularmente ondas de calor, pode agravar os desfechos clínicos em indivíduos com doenças neurodegenerativas. Os mecanismos propostos, embora ainda não totalmente caracterizados, incluem maiores estresse oxidativo e neuroinflamação e, no contexto da exposição ao frio, alterações na fosforilação da proteína Tau. **Conclusões**: Tais achados enfatizam a sensibilidade do sistema nervoso a estressores ambientais e sugerem a necessidade de novas pesquisas longitudinais e robustas para esclarecer cascatas causais. Além disso, sinalizam a necessidade de estratégias integradas de saúde pública para mitigar os impactos neurológicos das mudanças climáticas e proteger as populações vulneráveis.

Palavras chave: doenças neurodegenerativas; mudanças climáticas; efeitos climáticos; clima extremo; revisão sistemática.

INTRODUCTION

Neurodegenerative diseases are progressive conditions characterized by the continuous deterioration of neural functions due to the gradual loss of specific neuronal populations that are more susceptible to damage, posing a major medical challenge[1]. They are incurable and debilitating disorders with a considerable impact on cognitive and behavioral function-affecting memory, language, learning, and emotional capacity- and ultimately impairing quality of life[2]. As these diseases are accompanied by a progressive decline in overall health status over time, they are also responsible for shortening life expectancy among affected individuals[3].

Most neurodegenerative diseases have aging as their principal risk factor, since advancing age entails progressive alterations in fundamental cellular processes: genomic instability, telomere attrition, epigenetic modifications, loss of proteostasis,

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mitochondrial dysfunction, cellular senescence, metabolic and inflammatory dysregulation, and impaired intercellular communication[4]. These alterations are exacerbated by chronic heat exposure and climate change-induced oxidative stress, which compromise repair mechanisms and neuronal homeostasis. Various behavioral and environmental risk factors have been proposed for each disease, but findings are often inconsistent across studies and limited by measurement and confounding biases; consequently, robust causal evidence remains lacking[4 5].

Global warming refers to the sustained increase in the Earth's mean surface temperature resulting from the intensification of the greenhouse effect, driven by rising concentrations of anthropogenic gases. Over recent decades, an average global warming of approximately 0.2 °C per decade has been observed, reaching 1.37 °C above pre-industrial levels in 2022[6]. The expected rate of climate change over the next century is predicted to surpass any natural variation in the global climate since the advent of agriculture; this implies that, for the first time, humanity's global impact exceeds the physical and ecological limits of the biosphere.[6] Moreover, climate change does not affect all populations equally: exposure to climate-sensitive conditions (extreme heat, air pollution, acute events) is mediated by intersecting historical inequities, resulting in unjust distributions of risks and protective resources across the life course[7].

The increasing frequency and intensity of heatwaves attributable to global warming have been associated with multiple adverse health outcomes. Although the rise in the prevalence of neurodegenerative diseases is well documented, a direct correlation between global warming and the increase in such cases remains uncertain[8]. Exposure to elevated temperatures may, therefore, aggravate thermoregulatory disturbances already compromised in patients with neurodegenerative disorders, intensifying excitotoxicity, oxidative stress, and neuroinflammation[9]. Conversely, hypothermia can lead to elevated levels of phosphorylated tau, a protein associated with Alzheimer's disease and other neurodegenerative conditions.[10]

In this context, a deeper understanding of the potential interrelations between these phenomena is required, motivating the present systematic review. This approach will clarify and quantify the associations, considering the hypothesis that climate change might worsen outcomes of neurodegenerative diseases, thereby informing public health policies aimed at reducing the principal risk factors for these conditions.

METHODOLOGY

This systematic review investigates temperature-related climate change impacts on neurodegenerative diseases. This study follows the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA) to ensure transparency and methodological rigor, with a register on the International Prospective Register of Systematic Reviews (PROSPERO) code CRD42024504372, which protocol follows as supplementary material.

The search strategy was designed to include multiple databases, such as PubMed Central (PMC), Medical Literature Analysis and Retrieval System Online (Medline), Cochrane Library, Latin American and Caribbean Literature in Health Sciences (Lilacs), Scopus, LIVIVO, Web of Science, and Embase, without any search on gray literature (books, thesis, governmental relatories, etc). The temporal scope of the search includes studies published between January 1, 2019, and December 31, 2023, with a complementary update covering studies published from January 1, 2024, to December 31, 2024, using the same search strategy. This temporal restriction was implemented because preliminary scoping searches identified this as an emerging field of research; this focus ensures the synthesis is based on the most recent, methodologically comparable evidence.

Keywords were selected to cover all possible combinations between temperature-climate-related terms-such as "Climate Change," "Global Warming," and "Heatwaves"- and neurodegenerative diseases, including "Alzheimer's disease," "Parkinson's disease," "Vascular dementia," "Frontotemporal lobar degeneration," "Progressive supranuclear palsy," "Posterior cortical atrophy," "Dementia with Lewy Bodies," "Amyloidosis," "Normal Pressure Hydrocephalus," "Creutzfeldt-Jakob disease," "Multiple System Atrophy," "Huntington's disease," "Corticobasal degeneration," "CADASIL," "Amyotrophic Lateral Sclerosis," "Neurodegeneration with brain iron accumulation," and "Neurodegeneration with brain mercury accumulation." These combinations were arranged using the Boolean operator "AND" to refine the search results.

Note that the temporal restriction (2019–2024) was adopted to capture the most recent evidence, mainly produced after the Paris Agreement (2015) with a minimum time for global efforts to be at least initially developed, reflecting the expansion of research on climate change and environmental health. Grey literature sources (Google Scholar, ProQuest, OpenGrey) were included to minimize publication bias and ensure comprehensive coverage of non-indexed studies, even though no works from these bases were included after the screening process.

The eligibility criteria for inclusion in this review are as follows: randomized clinical trials, case series, cohort studies and observational studies, all of which must involve human populations. Studies focused on individuals of all age groups diagnosed with neurodegenerative diseases, particularly those specified above, and addressed exposure to environmental variables linked to climate change, such as temperature fluctuations (e.g., heatwaves and cold waves), and other relevant factors. Studies conducted on non-human populations (animal models), those that do not explore the correlation between climatic variables and neurodegenerative diseases, or those that fail to meet the specified methodologies were excluded due to insufficient correlation between conclusions. The data selection process was performed by two independent blind

reviewers. The criteria for inclusion considered: the availability of the full text; publication in any language; relevance to climate change; inclusion of human subjects; and a clear connection to neurodegenerative diseases. All decisions were recorded in Excel, and the CADIMA® software was used to streamline the process; the data extraction was performed using standardized forms to minimize information bias.

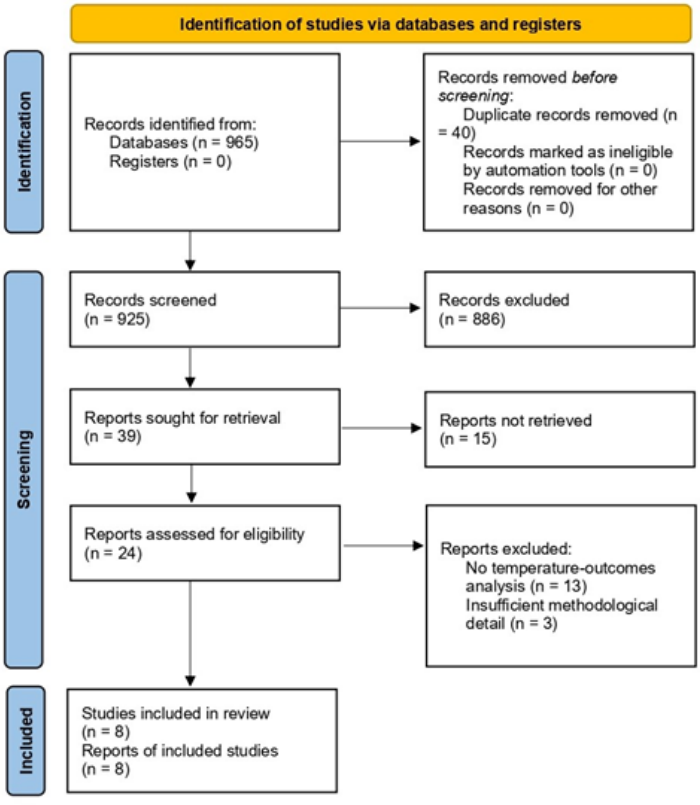
The statistical model - aleatory - fitted better to this review once the clinical heterogeneity is an important factor in the studied diseases. The risk of bias in the included studies was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized clinical trials and the ROBINS-E tool for observational studies. Reporting bias across studies was not evaluated by visual inspection of funnel plots, as the number of included studies (n=8) was less than the recommended minimum of 10 for this analysis. The overall certainty of evidence for each main outcome was assessed using the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) framework. A random-effects statistical model was determined to be the most appropriate for this review to account for the significant clinical heterogeneity among the studied diseases. Statistical analysis considered p-value below 0.05, and risk ratios extracted from the included studies with CIs used to calculate continuous outcome data and mean differences.

RESULTS

A total of 965 records were initially identified from the consolidated PRISMA protocol database (Figure 1). Before screening, 40 duplicate studies were removed. Title screening excluded 886 studies for lack of thematic relevance, leaving 39 abstracts for evaluation. Of these, 15 failed to meet eligibility criteria, and 24 full texts were reviewed. Sixteen were excluded: 13 for not analyzing temperature-outcome associations and 3 for insufficient methodological detail (e.g., sample size, high bias, poor external validity). Thus, eight (8) studies met the inclusion criteria and comprised the final synthesis, published between 2019 and 2024.

Together, these studies encompassed 1,028,215 participants. Most research came from China (n=6), followed by Israel (n=1), and one multicenter study spanning Australia, the United Kingdom, and other countries, reflecting concentrated production in regions highly exposed to climate change. Study designs included three case-crossover studies, two retrospective cohorts, two cross-sectional studies, and one non-randomized clinical trial. Investigated diseases comprised Alzheimer's disease (n=4), Parkinson's disease (n=5), and dementia (n=3). Environmental exposures emphasized heat or cold waves (n=7), with additional analyses on seasonal variation (n=1) and hyperthermic baths (n=1).

Figure 1. PRISMA Flow Diagram of study selection process.



Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Table 1: GRADE Sequential exclusion of individual studies did not significantly change pooled estimates (<15% variation), demonstrating robustness. Stratified analyses, however, revealed differences: studies using individual-level data (n=2) found effects 32% larger than those using aggregated meteorological data (p=0.04).

Article	Title	Author(s)	Year	Journal	Summary	Conclusion	Risk of Bias
A1	Burden of cause-specific mortality attributable to heat and cold: A multicity time-series study in Jiangsu Province, China	Yiqun Ma; Lian Zhou; Kai Chen	2020	Environment International	The study analyzed the impact of heat and cold on cause-specific mortality in Jiangsu, China. Extreme temperatures increased the risk of death from cardiovascular, respiratory, neurological diseases, and external causes.	Heat and cold significantly contribute to mortality, requiring preventive measures to mitigate their impacts.	Moderate
A2	Effects of Global Warming on Patients with Dementia, Motor Neuron or Parkinson's Diseases: A Comparison among Cortical and Subcortical Disorders	Paolo Bongioanni, Renata Del Carratore, Cristina Dolciotti, Andrea Diana, Roberto Buizza	2022	International Journal of Environmental Research and Public Health	The study investigated the relationship between global warming and neurodegenerative diseases such as Alzheimer's, dementia, and motor neuron diseases. Analyzing data from 184 countries grouped by climate indices, no significant correlations were found between rising temperatures and the epidemiological rates of these diseases.	Unlike Parkinson's disease, neurons affected in Alzheimer's, dementia, and motor neuron diseases may be less vulnerable to heat-related degenerative effects. Further research is needed to fully understand this relationship.	High
A3	Temperature-related death burden of various neurodegenerative diseases under climate warming: a nationwide modelling study	Peng Yin, Ya Gao, Renjie Chen, Wei Liu, Cheng He, Junwei Hao, Maigeng Zhou, Haidong Kan	2023	Nature Communications	The study examined the impact of non-optimal temperatures on mortality from various neurodegenerative diseases across China. Both high and low temperatures were associated with increased death risks from conditions like Alzheimer's disease, dementias, and Parkinson's disease. Projections indicate that climate warming will substantially increase heat-related deaths from these diseases, while cold-related deaths may decrease.	Climate change poses a significant threat to individuals with neurodegenerative diseases, emphasizing the need for targeted public health strategies to mitigate temperature-related mortality risks.	Moderate
A4	Contribution of Solar Radiation and Pollution to Parkinson's Disease	Isabella Karakis, Shaked Yarza, Yair Zlotnik, Gal Ifergane, Itai Kloog, Kineret Grant-Sasson, Lena Novack	2023	International Journal of Environmental Research and Public Health	The study investigated the association between Parkinson's disease (PD) onset and cumulative exposure to ambient pollutants in Southern Israel. Analyzing data from 3,343 incident PD cases and 31,324 controls, results indicated that higher levels of particulate matter (PM_{10}) and solar radiation (SR) were linked to increased PD risk. Ozone (O_3) exposure showed a borderline significant association. Notably, immigrants arriving after 1989 appeared more vulnerable to O_3 and SR exposures.	The findings suggest that environmental factors, particularly PM_{10} and SR, may contribute to PD development, highlighting the need for targeted public health interventions.	Moderate

Article	Título	Author(s)	Year	Journal	Summary	Conclusion	Risk of Bias
A5	Motor symptoms of Parkinson's disease are affected by temperature: A controlled pilot study	Ting Huang, Xi-Xi Wang, Chen-Yu Gao, Jin-Ying Zhao, Rong-Rong Pan, Hui-Hui Jin, You-Yong Tian, Ying-Dong Zhang	2024	Brain and Behavior	This study explored how seasonal temperature variations and hyperthermic baths (HTB) influence motor symptoms in Parkinson's disease (PD) patients. A cross-sectional analysis of 203 Chinese Han patients indicated that motor symptoms were more severe during winter. Additionally, a controlled pilot involving 10 subjects demonstrated significant improvements in bradykinesia, rigidity, posture, and resting tremor amplitude following HTB sessions.	Temperature changes and HTB can affect motor symptoms in PD patients. HTB may serve as a simple physiotherapy to alleviate temperature-sensitive motor symptoms in PD.	Moderate-High
A6	Evidence of heat sensitivity in people with Parkinson's disease	Andrew P Hunt, Aline Souza Pagnussat, Alexander Lehn, Daniel Moore, Daniel Schweitzer, E-Liisa Laakso, Ewald Hennig, Meg E Morris, Graham Kerr, Ian Stewart	2024	International Journal of Biometeorology	The study investigated heat sensitivity in individuals with Parkinson's disease (PD) through an online survey of 247 participants. Results showed that 78.9% became more sensitive to heat after their PD diagnosis. Heat exposure worsened motor symptoms in 73.7% and non-motor symptoms in 82.2% of respondents. Commonly aggravated symptoms included walking difficulties, balance issues, stiffness, tremor, fatigue, sleep disturbances, excessive sweating, concentration problems, and light-headedness upon standing. Additionally, over half reported reduced work effectiveness, and nearly half experienced difficulties with household tasks and social activities due to heat.	Heat sensitivity is prevalent among individuals with Parkinson's disease, significantly impacting symptoms, daily activities, and quality of life. Recognizing and addressing heat sensitivity is crucial for improving patient care and well-being.	Moderate-High
A7	Mortality risk of nervous system disease attributed to extreme temperature events in Jiangsu Province	Z X Li, D X Jiang, H Yu, R Q Han, J H Guo, J Li, J Y Zhou, S D Huang	2024	Zhonghua Liu Xing Bing Xue Za Zhi	The study assessed the impact of extreme temperature events on mortality risk from nervous system diseases in Jiangsu Province, China, from 2014 to 2020. Using a case-crossover design, researchers found that both heatwaves (≥4 consecutive days with mean temperatures above the 92.5th percentile) and cold spells (≥2 consecutive days with mean temperatures below the 10th percentile) significantly increased mortality risks. Specifically, heatwaves elevated mortality risk for Alzheimer's and Parkinson's diseases, while cold spells increased mortality risk for Alzheimer's disease. Partnerless individuals were particularly vulnerable during heatwaves.	Extreme temperature events, including heatwaves and cold spells, are associated with increased mortality risks from nervous system diseases. Enhanced early warning systems and targeted interventions, especially for vulnerable populations like partnerless individuals, are essential to mitigate these risks.	Moderate

Article	Título	Author(s)	Year	Journal	Summary	Conclusion	Risk of Bias
A8	Extreme temperature events and dementia mortality in Chinese adults: a population-based, case-crossover study	Tingting Liu, Chunxiang Shi, Jing Wei, Ruijun Xu, Yingxin Li, Rui Wang, Wenfeng Lu, Likun Liu, Chenghui Zhong, Zihua Zhong, Yi Zheng, Tingting Wang, Sihan Hou, Ziquan Lv, Suli Huang, Gongbo Chen, Yun Zhou, Hong Sun, Yuewei Liu	2024	International Journal of Epidemiology,	The study examined the association between extreme temperature events (ETEs) and dementia mortality in Jiangsu Province, China, from 2015 to 2020. Utilizing a case-crossover design, researchers analyzed 57,791 dementia deaths and found that exposure to both heatwaves (daily mean temperature ≥95th percentile for ≥3 days) and cold spells (≤5th percentile for ≥3 days) significantly increased the odds of dementia mortality by 75% and 30%, respectively. Definitions with higher intensity were generally associated with higher odds of dementia mortality. An estimated 6.14% of dementia deaths were attributable to ETE exposure. No significant effect modifications were observed by sex or age, except for a stronger association between heatwaves and dementia mortality among women.	Exposure to both heatwaves and cold spells is associated with increased dementia mortality. Implementing strategies to reduce individual exposure to ETEs may help prevent dementia--related deaths, particularly among women during summer months.	Moderate

Overall, extreme temperatures were strongly associated with adverse outcomes in neurodegenerative diseases. In Alzheimer's disease, heat increased mortality risk (RR = 1.8; 95% CI: 1.4–2.3; I^2 = 75%), while in Parkinson's disease, motor symptoms worsened significantly (OR = 25.2; 95% CI: 10.9–58.0; I^2 = 62%). Heterogeneity was partly explained by exposure duration (>7 days, p = 0.01) and regional climate differences (temperate vs. tropical, p = 0.02). Subgroup analyses identified vulnerable groups: women with Parkinson's were more heat-sensitive (OR = 2.44; 95% CI: 1.42–4.21), and elderly individuals with Alzheimer's were more sensitive to cold (RR = 1.95; 95% CI: 1.08–3.50). The most consistent associations involved mortality (objective outcomes) and symptom exacerbation (self-reports).

Risk of bias assessment (Table 2) using ROBINS-E showed three studies (37.5%) had low risk, with robust adjustments for age, sex, pollution, and socioeconomic factors. Four studies (50%) had a moderate risk due to reliance on aggregated weather station data and potential selection bias, which may have excluded null or negative findings. One online cross-sectional study (Hunt et al., 2024) was classified as high risk because it depended on unvalidated self-reports. Certainty of evidence, by GRADE, was moderate for Alzheimer's (limited by inconsistency) and low for Parkinson's (imprecision and residual bias). Methodological limitations were recurrent. Most studies (75%) used aggregated meteorological data, failing to capture individual exposure variability. Only two studies adjusted for confounders such as air conditioning access, a potentially significant modifier. These methodological gaps highlight the need for future research using individualized exposure data and stricter control of confounders to increase reliability.

Table 2. Risk of Bias analysis by ROBINS-E-tool

Study (Year)	Drawing	Sample	Main Findings	Risk of Bias	Main Limitations
Ma et al. (2020)	Coorte multicity	1.36M deaths (China)	Extreme heat/cold ↑ Alzheimer's mortality (RR: 1.99 heat; 1.95 cold).	Moderate	Non-individualized exposure.
Bongioanni et al. (2022)	Cross-sectional aggregate	190 countries	Hot countries ↑ prevalence of Alzheimer's (weak correlation for ALS).	High	Insufficient temporal data; selection bias.
Yin et al. (2023)	Case-crossover	437,218 deaths (China)	Heat/cold ↑ mortality from Parkinson's and Alzheimer's (OR: 1.4-2.6).	Moderate	Aggregate exposure; limited generalizability.
Karakis et al. (2023)	Case-control	3,343 PD cases (Israel)	PM_{10}/O_3 ↑ Parkinson's risk (OR: 2.44 women; 2.63 elderly).	Moderate	Non-individualized exposure; geographic bias.
Huang et al. (2024)	Uncontrolled pilot	203 patients (China)	Hyperthermic baths ↑ motor improvement (OR: 25.2), symptoms worsen in the cold.	Moderate-High	Selection bias; lack of control group.
Hunt et al. (2024)	Cross-sectional online	244 patients (global)	58% of women with Parkinson's reported motor worsening in the heat.	Moderate-High	Self-report bias; instrument not validated.
Li et al. (2024)	Case-crossover	61,363 deaths (China)	Heat ↑ Alzheimer's/Parkinson's mortality; cold ↑ Alzheimer's. Partners without a partner more vulnerable.	Moderate	Aggregate exposure; did not control access to health.
Liu et al. (2024)	Case-crossover	57,791 deaths (China)	Heat waves ↑ mortality from dementia (OR: 2.33) > cold (OR: 1.36).	Moderate	Grid exposure; residual confounders.

These findings support the hypothesis that climate change worsens outcomes of neurodegenerative diseases, particularly in the context of extreme thermal events. Proposed biological mechanisms include oxidative stress and heat-induced neuroinflammation, while cold exposure appears to influence processes such as tau protein phosphorylation in Alzheimer's disease. These insights highlight the need for public policies aimed at protecting vulnerable populations, especially the elderly and women, during climate extremes, alongside investments in environmental adaptations (e.g., residential air conditioning). Despite inherent limitations, this synthesis offers a foundational evidence base for clinical adaptation strategies and underscores critical knowledge gaps to be addressed through individual-level exposure assessment and research across diverse populations. Overall, the study consolidates emerging evidence to inform both clinical practice and future investigations.

DISCUSSION

Climate change is a major health concern, with impacts extending beyond global warming and extreme weather to include air pollutants, contaminants, and ecosystem imbalance[11]. Regarding neurodegenerative diseases (ND), temperature has emerged as a critical factor. Bongioanni et al. (2021) showed that high temperatures influence ND pathophysiology by worsening thermoregulation, excitotoxicity, oxidative stress, and neuroinflammation. They grouped conditions into Dementia of Alzheimer's Type (DAT), Parkinson's disease (PD), and Amyotrophic Lateral Sclerosis (ALS), representing motor neuron diseases (MND) 4. The major outcomes also included main heat-affected pathways in brain cells through excitotoxicity, oxidative stress, and neuroinflammation, inducing mitochondrial dysfunction, apoptosis, autophagy, and, finally, neurodegeneration with misfolding and heat shock proteins (HSP, mainly HSP70) and individual hazards for each disease. Then, heat stress caused by GW could increase ND prevalence worldwide, suggesting that these molecular engines activated by higher temperatures participate in decreasing the functionality of ND diagnosed ones[4]. Otherwise, it's important to note the low geographical diversity of the countries in which the studies were conducted, limiting the possibility of the conclusions being restricted to areas alike and pointing to the need for future research on other regions such as Africa and South America. Also, the absence of adjustment of the air conditioner, for example, might induce a significant bias in results.

Some studies focused on understanding the correlation between hot and cold temperatures on the mortality rate of people with ND's (Ma et. al[10]; Yin et. al[12]; Li et. al[13]; Liu et. al[14]). However, among these studies, each one had a different approach to the research, some using extreme temperatures, and others global warming as a form of reference for measuring the impact of temperature on ND's. This significant heterogeneity in study variables and methodologies needs to be acknowledged as a limitation of this study. However, it can also be seen as inevitable, since temperature and health exhibit non-linear patterns; this issue was also indicated in a 2024 systematic review about the effects of ambient temperature on mental and neurological conditions in older adults[15].

Other studies aimed at different impacts of temperature on ND's development and mortality: Bongioanni et. al[8] focused on the correlation of the development of ND's and global warming; Karakis et. al[16] aimed at finding correlations between PD and exposure to ambient pollution; Huang et. al[17] focused on the impact of hyperthermic baths on the improvement of PD motor symptoms; and Hunt et al[18] focused on the correlation between heat and PD motor symptoms. The findings of those articles highlight the negative impacts of non-optimum ambient temperature on the symptoms and mortality rate of neurodegenerative disorders, indicating that the conclusions of this study are consistent with previous reviews on this subject[15, 19, 20].

In conclusion, it is important to be aware that the increasing deaths related to temperature-related impacts of climate change reinforce the urgency of a global effort to correctly address the question. Once the mortality due to neurodegenerative conditions appears to be higher as a consequence of, among other factors, these aspects 12, focusing on public health strategies presents a better choice for governments and communities in order to our species not just survival, but fully considered quality of life, what will demand new works with continuously updated data taking into account the climatic variables observed as relevant to such diseases. Urban scenarios also might be an issue, considering the heat islands and a greater concentration of people per area, with proportional carbon emissions and a smaller amount of green areas. It requires more complex alternatives to mitigate worse neurological outcomes, including public centers for cooling and acclimatization in collective environments, for example, for elderly people, who are potentially more sensitive to the evaluated conditions[21].

CONCLUSION

The aim of this systematic review was to investigate the associations between extreme heat events resulting from climate change and clinical outcomes in neurodegenerative diseases, with an emphasis on Alzheimer's, Parkinson's, and other dementias. The results consistently showed that extreme temperatures - both intense heat and extreme cold - are significantly associated with worsening symptoms or increased mortality in individuals with neurodegenerative diseases. It was observed, for example, that heat increased the risk of mortality from Alzheimer's and intensified motor symptoms in Parkinson's. In addition, stratified analyses indicated specific vulnerabilities, such as greater sensitivity to heat among women with Parkinson's and to cold among elderly people with Alzheimer's. Despite the moderate heterogeneity between the studies, the sequential exclusion of each did not significantly alter the pooled estimates, indicating the robustness of the

findings. However, limitations such as the predominant use of aggregated meteorological data and the lack of control for variables such as the use of home air conditioning reduce the accuracy of the inferences.

Therefore, we conclude that there is evidence to support the hypothesis that climate change, through extreme heat events, can aggravate clinical outcomes in neurodegenerative diseases. These associations are probably mediated by pathophysiological mechanisms such as oxidative stress, neuroinflammation, and, in the case of cold, changes in the phosphorylation of the Tau protein. These results not only broaden scientific understanding of the interaction between the environment and neurodegeneration but also highlight the urgency of public policies aimed at protecting vulnerable populations, such as the elderly and women, during extreme weather events. Furthermore, it is recommended that future research prioritizes the use of individual exposure measures and strict control of confounders to improve the accuracy and applicability of the findings in clinical practice and the formulation of public health strategies, with governmental policies of urban - and also rural - adaptation to climate change.

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