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Sleep disturbances and their relation to dementia in Alzheimer's disease: A systematic review according to the PRISMA Statement

Alteraciones del sueño y su relación con la demencia en la enfermedad de Alzheimer: de acuerdo con la Declaración PRISMA

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SUMMARY

The objective of this research was to establish relationships between the occurrence of sleep disorders and the development of Alzheimer's disease. The methodology employed was a systematic review conducted according to the PRISMA method utilizing the Scopus, PsycINFO, and Web of Science databases. The keywords used were sleep disturbances, dementia, and Alzheimer's disease. The sample consisted of 31 scientific articles, selected according to the established inclusion criteria. The most important findings highlight the significant relationship between sleep disturbances and Alzheimer's disease. Scientific studies indicate that changes in the sleep cycle typically occur in the early stages of the disease, manifesting as difficulties falling asleep, nighttime interruptions, and insomnia. These alterations impact the lives of adults and are diagnostic indicators in the progression of dementia.

Keywords: *Systematic review, sleep disturbances, dementia, Alzheimer's disease.*

RESUMEN

El objetivo de esta investigación fue establecer relaciones entre la presentación de trastornos del sueño y el desarrollo de la enfermedad de Alzheimer.

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La metodología empleada fue una revisión sistemática según el método PRISMA utilizando las bases de datos Scopus, PsycINFO, y Web of Science. Las palabras clave utilizadas fueron: alteraciones del sueño, demencia, pacientes con enfermedad de Alzheimer. La muestra estuvo compuesta por 31 artículos científicos, seleccionados de acuerdo con los criterios de inclusión establecidos. Los hallazgos más relevantes resaltan la significativa relación entre las alteraciones del sueño y la enfermedad de Alzheimer. Los estudios científicos evidencian que las modificaciones en el ciclo de sueño suelen presentarse en las primeras etapas de la enfermedad, manifestándose como dificultades para conciliar el sueño, interrupciones nocturnas e insomnio. Estas alteraciones impactan la vida de los adultos y son indicadores diagnósticos en la progresión de la demencia.

Palabras clave: *Revisión sistemática, alteraciones del sueño, demencia, enfermedad de Alzheimer.*

INTRODUCTION

Over time, people experience significant age-related changes that impact both their physical appearance and cognitive abilities. These changes may manifest as difficulties in specific areas of development, with memory loss being one of the most common impairments. This condition may be linked to attention problems, as well as emotional factors and stress (1). Additionally, alterations associated with the deterioration of the central nervous system may be a consequence of aging or pathologies that contribute to this process.

Dementia associated with Alzheimer's disease is characterized by the loss of cognitive abilities and skills in older adults. This pathology interferes with the basic daily activities of those who suffer from it since it is a neurodegenerative disease that causes a progressive deterioration of functionality. It affects brain areas linked to the cortex and hippocampus (2).

The most frequent symptoms of Alzheimer's disease are related to short-term memory loss, although impairment in long-term memory storage is also observed. This symptomatology can manifest itself in most patients. Over time, problem-solving ability deteriorates, and judgment is impaired, leading to a loss of coherence with respect to their reality. Another important alteration is the dysfunction of executive processes and disorganized thinking (3).

On the other hand, the impairment of executive processes varies from mild to chronic. Manifestations include language impairment and loss of visuospatial skills. In addition, neuropsychiatric symptoms are observed, such as decreased emotional expression, apathy, mood changes, and anhedonia. Motor symptoms may also be present, such as dyspraxia, which refers to difficulties in carrying out previously learned motor activities (4).

It is essential to point out that the central nervous system interacts with several psychological variables. When there are alterations in the functioning of neurotransmitters, distortions arise that affect adaptation to the environment, as well as negative behaviors and emotions that evidence the deterioration of the patient with Alzheimer's disease. As a result, discomfort and behavioral patterns of disinhibition occur (5).

Another important aspect of Alzheimer's disease is sleeping disturbances, which constitute a disruptive symptomatologic form. These disturbances significantly impact the patient's cognitive functions and overall functionality. In general, older adults tend to take longer to fall asleep but may awaken more easily. As a result, they often experience nighttime sleep disruptions more frequently (6,7).

Changes in sleep performance and sleep quality appear to precede the first signs of cognitive impairment in patients with Alzheimer's disease. These alterations are progressive and intensify as the disease progresses. As a result, a mismatch in the circadian rhythm of sleep and a decrease in the deep sleep phase and efficiency significantly impact sleep quality (8).

On the other hand, it is important to note that many people do not practice physical activities when they reach a certain age, due to occupations or inactive lifestyles, physical activity promotes benefits such as improving sleep patterns, and allows adequate oxygenation of the central nervous system, helping cardiovascular function, another area favored are the cognitive elements related to executive functions, their contributions prevent physical and cognitive diseases (9).

Considering the evidence, the following research question is generated: How are sleep disorders related to the development of Alzheimer's disease? Thus, this study aimed to establish the relationships between occurrence of sleep disorders and the development of Alzheimer's disease.

METHOD

The PRISMA method was employed in elaborating this work, due to its scientific rigor, which enables the collection of information from various scientific documents found in open-access databases detailed in the research work (10) (Figure 1).

The approach of this study is based on quantitative parameters and is characterized by its nature as an exploratory systematic review, theoretically based on the PRISMA statement (2020). Additionally, procedures utilizing Boolean operators were implemented to optimize the search and organization of the work, ensuring an exhaustive and relevant compilation of the existing literature in the field of study.

The selection, analysis, and codification of the information from the referent texts disclosed in various scientific journals and their location are identified within the category of open access (using the OJS system). Scopus, PsycINFO, and Web of Science databases allow for the relation of different studies that thoroughly explore a specific topic to explain the related realities.

The search was focused on the categories of analysis indicated: sleep disturbances, dementia, and Alzheimer's disease. The sample comprises 31 scientific research papers selected from primary and secondary sources, covering the last 5 years (2019-2024) and encompassing research in both Spanish and English.

The database exploration processes were conducted using Scopus, PsycINFO, and Web of Science, applying Boolean operators such as AND, OR, and NOT according to predefined equations. This systematic approach ensured an exhaustive and relevant compilation of scientific literature related to the interest categories (Table 1).

Table 1. Equations.

Equations
"Alteraciones del sueño" and "Demencia" or = "Enfermedad de Alzheimer" not = "Niños" "Trastornos oniricos" and "Problemas Memoria" or Conducta"" not = "Adolescentes" "Dificultades" and "vigilia" or "Evocacion Informacion " not "Jovenes" "Deficit" and "cognitivo" or "insomnio" not infancia "Deterioro" and "neurogenetaivo" or "Acto de dormir" or "Vejez" not "neurodesarrollo" "Sleep disorders" and "Dementia" or = "Alzheimer's disease" not = "Children" "Dream disorders" and "Memory problems" or = "Behavior" not = "Adolescents" "Difficulties" and "wakefulness" or "Information recall" not "Youth" "Deficit" and "cognitive" or "insomnia" not "childhood "Deterioration" and "neurogenetic" or "Act of sleeping" or "Old age" not "neurodevelopment"

Search strategies and criteria

Tables 2,3,4, and 6 present the search and collection process and the inclusion and exclusion criteria for the sample of scientific texts. The search procedure and data collection process are also highlighted. The strategy used for data collection was based on criteria that included the following elements: characteristics of the works, subject of interest, time period, and variables (11). This procedure increases the probability of obtaining more reliable results while minimizing the risk perspective in selecting and analyzing the reviewed literature.

Table 2. Inclusion and exclusion criteria.

Search procedure	Data collection process	Exclusion criteria	Inclusion criteria
An initial survey was conducted through open-access databases, considering articulation, contributions, and research results directly related to the subject of review, with a focus on the last 5 years. The selected languages were English and Spanish. Variables related to sleep disturbances and their relationship with dementia in Alzheimer's disease were examined.	We conducted a search using the PRISMA methodology, ensuring that the selected documents contribute to the field of knowledge relevant to the study variables. To achieve this, we worked with synonyms of the concepts to identify a high number of characteristics and relevant studies addressing the problem question (Figure 1).	Works that meet the following criteria: - Reflective research texts. - Books or book chapters. - Essays. - Those works that do not contribute to the research variables.	Research texts with the following criteria: - Research within the last 5 years. - Scientific texts in Spanish and English languages. - Documents articulated with the research variables.

Table 3. Cross-referencing of search terms in databases.

Search	Databases	Final Result			
"Alteraciones del sueño" and "Demencia" or = "Enfermedad de Alzheimer" not = "Niños" "Trastornos oniricos" and "Problemas Memoria" or Conducta"" not = "Adolescentes" "Dificultades" and "vigilia" or "Evocacion Informacion " not "Jovenes" "Deficit" and "cognitivo" or "insomnio" not infancia "Deterioro" and "neurogenetaivo" or "Acto de dormir" or "Vejez" not "neurodesarrollo" "Sleep disorders" and "Dementia" or = "Alzheimer's disease" not = "Children" "Dream disorders" and "Memory problems" or = "Behavior" not = "Adolescents" "Difficulties" and "wakefulness" or "Information recall" not "Youth" "Deficit" and "cognitive" or "insomnia" not "childhood "Deterioration" and "neurogenetic" or "Act of sleeping" or "Old age" not "neurodevelopment"	Scopus	1 080	900	1 360	1 150
	PsycINFO	850	382	782	650
	Web of science	750	958	292	1 580
	Total	2 680	2 240	2 434	3 380

Table 4. Results total number of texts per database

Databases	Final result
Scopus	4 490
PsycINFO	2 664
Web of Science	3 580
Total	10 734

Considering the search performed, a specific range of works was identified in each database, which offer significant contributions to the execution and constitution of the exploration of the documents. Based on the above, the detailed texts were organized and transferred to a flow chart to facilitate the data extraction process. This flowchart provides a clear visualization of the workflow, ensuring that each stage of the information gathering and analysis process is systematic and orderly, thereby optimizing the quality and relevance of the extracted data.

Selection of the studies

In selecting the documents (Table 5), a time period of the last five years was considered, articulating the specific variables of the research work. In this sense, direct-access databases were selected, and duplicate scientific documents were excluded. Additionally, priority was given to texts that demonstrated coherence with the research variables. Only complete scientific papers were used, avoiding the inclusion of abstracts and research notes (12).

Table 5. Process of identification, elimination, and selection of items

Boolean operators	Algorithm AND, OR y NOT			
Number of Articles in Language	Spanish		English	
	7 354		3 380	
Databases	Scopus	PsycINFO	Web of science	Total
No filter	3 780	3 380	3 574	10 734
No access	1 680	1 600	1 800	5 080
Revisions/incomplete/ duplicates	1 250	1 050	1 100	3 400
Does not meet criteria	668	631	924	2 223
Selection	10	9	12	31

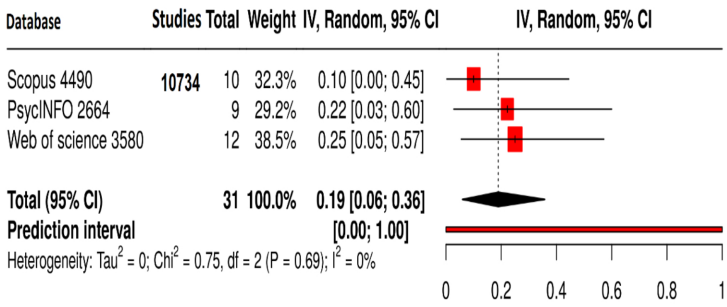
Data extraction

This process is elaborated with the objective of identifying the selected scientific studies, later to place a filter for the duplicated and eliminated studies, therefore the next step is the pre-selection of documents, to find the complete scientific texts that contribute to the work, finally the complete research that has a meeting point with the proposed research variables are used.

Data meta-analysis

As shown in Table 6, a total of 3 databases were analyzed, containing a total of 10,734 studies. From these, a sample of 31 studies relevant to the research variables was selected, indicating reliable research. The analysis was performed using a random-effects model, considering the variance characteristics. The laconic ratio was set at 0.62, with a 95 % confidence interval ranging from 0.58 to 0.66. This methodological approach reinforces the credibility and robustness of the findings obtained in the review.

Table 6. Meta-analysis.



RESULTS

We conducted a search using the PRISMA methodology, ensuring that the selected documents contribute to the field of knowledge relevant to the study variables. To achieve this, we worked with synonyms of the concepts to identify a high number of characteristics and relevant studies addressing the problem question (Figure 1). A total of 10 734 references were found, and 31 references were finally selected (Table 5). In Table 7 are presented the Characterization of the studies included in the systematic review.

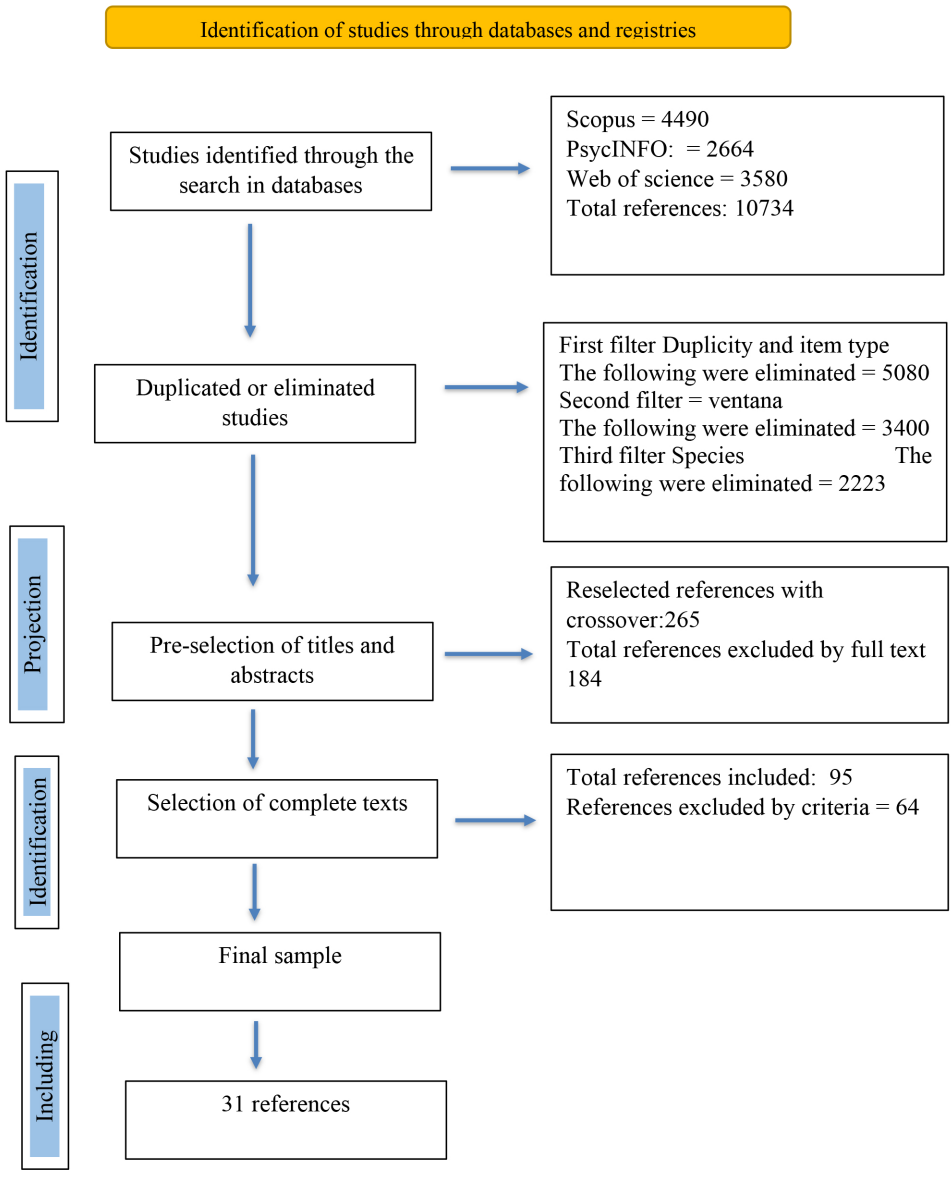


Figure 1. Study selection flowchart.

Table 7. Characterization of the studies included in the systematic review.

N	Authors and year	Keywords	Journal	Main results
1	Zhou et al. (13)	Alzheimer disease, sleep disorders symptoms of dementia, cognitive function.	Medicine	Sleep disorders significantly impact cognition and quality of life and increase apathy. This is very useful for future research on therapeutic targets in the clinical area.
2	Wu et al. (14)	Alzheimer disease, stress, sleep.	Frontiers in neuroendocrinology	This research highlights the relationship between sleep and circadian rhythm in the formation of stress granules, which represents a mechanism in the pathogenic process of Alzheimer's disease.
3	Stankeviciute et al. (15)	Alzheimer's disease, dementia, mild cognitive impairment, Sleep.	Journal of Sleep Research	Memory influences the subjective assessment of sleep in people with initial memory impairment.
4	Djonlagic et al. (16)	Aging; longitudinal analysis; memory.	Journal of sleep research	These findings support the idea that sleep may be a promising biomarker for detecting cognitive impairment.
5	Chen et al. (17).	Alzheimer's disease, Neuronal oscillation disturbance, Neuroinflammation	Neuroscience	There is a bidirectional relationship between Alzheimer's disease and sleep disorders. However, despite various pharmacological and non-pharmacological approaches, more research is still needed.
6	Bugalho and Salavisa (18)	Dementia, REM sleep behavior disorder.	Journal of Clinical Sleep Medicine	Having a sleep disorder contributes to the greater severity of motor events.
7	Lozano-Tovar et al. (19)	Alzheimer's disease, neuro-psychiatric symptoms, sleep disturbances.	Chilean journal of neuropsychiatry	Sleep disturbances are considered a risk factor associated with aging and the development of diseases such as Alzheimer's disease.
8	Cañas-Lucendo et al. (20)	Behavioral symptoms, Alzheimer's disease.	Psychological therapy	Evidence shows that the neurobehavioral profile most frequently affected in people without cognitive impairment is related to anxiety, apathy, sleep disturbances, and depression that differ significantly from Alzheimer's patients.
9	Tadokoro et al. (21)	Alzheimer's disease, oxidative stress.	International journal of molecular sciences	Oxidative stress is emerging as a relevant therapeutic target. New antioxidant supplements could offer hope in the prevention of dementia.
10	Koren et al. (22)	Dementia, Sleep, Insomnia.	Ageing Research Reviews	Sleep disorders are common in people with dementia. Moreover, despite twenty years of research, no progress has been made in the treatment provided.
11	Most et al. (23)	Alzheimer's dementia, sleep disturbance, healthy elderly.	The American Journal of Geriatric Psychiatry	The authors of this study emphasize that sleep is affected in the early and moderate stages, although the sleep-wake rhythm remains unchanged in healthy subjects.
12	Webster et al. (24)	Dementia, disturbance, qualitative research, sleep.	International Psychogeriatrics	Sleep disorders have a negative impact on residents with dementia. They affect people's physical and mental health, as well as their ability to manage their behavior and enjoy their daily lives.
13	Van Erum et al. (25)	Alzheimer's disease, Sleep physiology.	Neuroscience & Biobehavioral Reviews	Sleep disturbances significantly impact patients' ability to self-care, as well as caregiver burnout and institutionalization rates. Restoring an effective sleep-wake cycle in these patients remains an unsolved challenge, in part due to the complexity of sleep physiology and the interaction of multiple neurotransmitter systems.
14	Levendowski et al. (26)	Neurodegeneration, head position, sleep.	Journal of Alzheimer's Disease	This study demonstrates the utility of home sleep measurements in establishing the relationship between the supine sleeping position and neurodegenerative disorders.

Continued in page S333 …

…continuation Table 7. Characterization of the studies included in the systematic review.

N	Authors and year	Keywords	Journal	Main results
15	Pyun et al. (27)	Sleep disorders, behavior disorders, Circadian rhythm, and Alzheimer's disease.	Journal of Alzheimer	Subjects with Sundown syndrome have an increased likelihood of experiencing sleep behavior disorders related to rapid eye movements.
16	Poaquiza and Manzano (28)	Dementia, cognition, old age, and sleep.	Latam: Latin American Journal of Social Sciences and Humanities	No correlation was found between sleep quality in older adults and their cognitive functioning.
17	Gutiérrez et al. (29)	Alzheimer's disease; sleep, cognition.	Young people in science.	Studies on Alzheimer's disease in humans and animal models corroborate a possible causal association between Alzheimer's disease and sleep disruption.
18	Ferini-Strambi (30)	Dementia, sleep disorders	European Journal of Neurology	Further study and research should be focused on sleep disorders as a warning sign of possible early neurodegeneration.
19	Damsgaard et al. (31)	Dementia,epidemiology,sleep–wake disorders.	European Journal of Neurology	Sleep disturbances may be an early symptom of dementia. However, more studies are needed to differentiate these disorders as early indicators of the disease clearly.
20	Winer et al. (32)	Aging, Sleep, cognition.	JAMA neurology	The connection between sleep duration and several interrelated health outcomes, such as increased Aβ burden, depressive symptoms, elevated body mass index, and cognitive decline, underscores the importance of maintaining adequate sleep in old age.
21	Rescinitiet al.(33)	Dementia, insomnia, older adults, sleep, cognitive impairment.	International Journal of Environmental Research and Public Health,	This study emphasizes the urgent need to recognize sleep disturbances and their variations over time as risk factors for dementia.
22	Novak and Deshpande (34)	Sensory information in young and older adults.	Journal of the American Geriatrics Society	As subjects age, the prevalence of comorbid conditions affecting peripheral sensations increases, potentially exacerbating age-associated deterioration.
23	Xu et al. (35)	Sleep, cognitive deterioration, dementia.	Journal of Neurology, Neurosurgery & Psychiatry	Sleep regulation could be considered an effective approach to prevent dementia.
24	Tsai et al. (36)	Alzheimer's, sleep, treatment.	The Laryngoscope	Sleep apnea intervention decreases the risk of developing Alzheimer's disease in patients with this condition.
25	Sabia et al. (37)	Sleep, old age, dementia.	Nature communications	These researchers recommend that a short sleep duration is associated with an increased risk of dementia.
26	Wunderlin et al. (38)	Sleep, dementia, aging.	Psychiatry Research: Neuroimaging	Acoustic stimulation can be a valuable and noninvasive resource for intervening in cognitive impairment and improving slow-wave sleep disturbances.
27	Marde et al. (39)	Alzheimer's disease, Light therapy, Actigraphy; Polysomnography; Sleep disorder;	Asian Journal of Psychiatry	Non-pharmacological treatments, such as sleep education programs, Peter Hauri's rules, and light therapy, have been shown to play a key role in regulating sleep.
28	Phan & Malkani (40)	Alzheimer's disease, Sleep disorders.	Neurobiology of stress,	Circadian rhythm disturbance and stress worsen Alzheimer's disease pathology. Therefore, clinical interventions should introduce novel knowledge to approach from different perspectives.
29	Katsuki et al. (41)	Sleep disorders, Alzheimer's disease, neurons.	Brain research bulletin	Worldwide, Alzheimer's disease is considered one of the major public health challenges. Therefore, the identification of reliable biomarkers for the early detection of Alzheimer's disease is urgently needed.
30	Han et al. (42)	Sleep deprivation, Disease progression Risk factor. Alzheimer's disease.	Heliyon.	Current scientific studies demonstrate the implication of sleep deprivation in the onset and progression of Alzheimer's disease.
31	Delic et al. (43)	Alzheimer's disease, sleep deprivation, post-traumatic stress disorder.	Journal of Alzheimer's Disease	In this study, researchers suggest the existence of a strong relationship between sleep deprivation and Alzheimer's disease.

Relationship of sleep disturbances to cognitive function

Sleep disturbances significantly affect cognitive processes, including memory. During the day, episodes of daytime sleepiness impact executive functions, especially attention, resulting in a decrease in these capacities. This generates difficulties in recording and storing information adequately and concentrating and processing the information necessary to respond coherently to the search for previously recorded data (41).

One of the alterations associated with sleep loss is a significant decrease in cognitive performance, particularly in second-level processes related to inhibitory control. Patients facing sleep difficulties experience a progressive loss of these functions and cognitive flexibility, which is essential for regulating thinking and responding appropriately. As a result, patients with sleep disturbances are impaired in their ability to consistently develop reasoning and behavioral planning skills (44,45).

Influence of dementia on sleep disturbances

Sleep disorders can arise from neurological disturbances or impairments in the brain centers that control sleep. Therefore, these disorders are frequently related to sleep apnea, circadian rhythm, and rapid eye movement disorders. All of these disturbances are linked to neurodegenerative conditions; that is, as more disturbances occur in the central nervous system, people are at greater risk for sleep disorders (46).

Dementia's impact on sleep disturbances results from neuronal degeneration in the subcortical areas that regulate the sleep-wake cycle, leading to an abnormal sleep structure. This causes alterations in the REM phase and sleep characteristics. It is important to highlight that these affectations can lead to alterations in consciousness, affecting mental processes and generating changes in sensory perception. The neurodegeneration associated with dementia promotes variations in sleep, which can sometimes lead to sleep disorders (47).

Sleep disturbances and other pathologies

Sleep disturbances accelerate neurodegenerative disorders, playing a key role in the pathogenesis of these conditions. Sleep deprivation affects people's performance, as well as their cognitive abilities and skills, and can lead to disorders related to anxiety and depression. These dysfunctions impede the development of adequate emotional responses to various situations and affect decision-making, a crucial aspect at any stage of human development. It is important to note that these failures contribute to the inability to adapt and to the cognitive distortions that can occur (48).

Sleep is essential for overall health, and sleep disturbances are often linked to various health problems and disorders. Lack of proper sleep hygiene, such as not getting enough sleep, increases the risk of blood pressure problems, cardiac dysfunction, and alterations in eating behavior, such as excessive food consumption, which can lead to obesity. Additionally, these alterations can impact thyroid function and contribute to the development of diabetes (49).

Other pathologies that may arise are related to emotions. Lack of sleep can cause mood changes, making it difficult to adapt to various environments and different spheres of development. In this context, anxiety, anguish, and depression become risk factors that can lead to suicidal thoughts or even to the act itself as a way of alleviating the crises generated by these conditions (50). Also, loss of sleep quality is related to sexual function. Not getting adequate rest generates changes that affect hormonal balance, and exhaustion and chronic fatigue can negatively impact sexual performance (51).

DISCUSSION

In progressive neurodegenerative diseases such as Alzheimer's disease (AD), sleep disturbances can manifest at any stage of the disease, although they are more frequent in its early stages. It is important to note that these

disorders not only affect the quality of nighttime sleep but can also occur during the day, altering the regularity of the sleep-wake cycle. The most common symptoms include difficulties in falling asleep, sudden nocturnal interruptions, and insomnia characterized by early awakening, among other related alterations (52).

In addition, sleep disturbances may serve as a diagnostic indicator of pathologies associated with AD in the context of the onset of dementia. These disorders tend to worsen over time, and their intensity in the late stages of AD may be a predictive sign of mortality. The relationship between AD and sleep disorders is complex, suggesting the possibility of interventions from various perspectives (53). Although some studies, such as those by Gutierrez et al. (29), suggest a connection between sleep disruption and Alzheimer's disease (AD), indicating a possible causal relationship, further research is necessary to better understand the underlying mechanisms.

Sleep quality is crucial since insufficient or suboptimal rest has negative repercussions on mental health and the central nervous system, thus increasing the risk of cognitive impairment. On the other hand, the causes of AD are multifactorial; there are non-modifiable risk factors, such as genetic predisposition, along with those that can be altered through healthy lifestyle habits (54).

CONCLUSION

This research highlights the significant relationship between sleep disturbances and neurodegenerative diseases, particularly Alzheimer's disease. Research has shown that changes in sleep patterns can manifest at any stage of the disease, being more frequent in its early stages. These alterations, which include difficulties in falling asleep, nighttime interruptions, and symptoms of insomnia, not only affect the quality of life of patients but can also serve as important diagnostic indicators in the progression of dementia.

As the disease progresses, sleep disturbances tend to intensify, suggesting a complex interaction between the two phenomena. Evidence suggests that sleep quality is crucial for maintaining mental health and optimal central nervous system functioning; its deterioration may increase the risk of cognitive impairment. This implies that sleep disorders have a significant impact on cognition and the ability to perform daily activities and may also increase apathy in this population.

Crucially, sleep disturbances also impact patient self-care capacity and caregiver burnout. Therefore, restoring an effective sleep-wake cycle in these patients is an unsolved challenge, in part due to the complexity of sleep physiology and the interaction of multiple neurotransmitter systems.

It is essential to consider both non-modifiable risk factors, such as genetic predisposition, and those that can be addressed through healthy lifestyle habits. Sleep disorders negatively affect the physical health and quality of life of subjects with dementia. Future research should focus on exploring effective interventions that improve sleep quality in these patients, as this could have a significant impact on disease progression and the quality of life of those affected.

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