67° CONGRESSO NAZIONALE SIGG
"LA LONGEVITA' DECLINATA AL FEMMINILE"

Roma, 2 Dicembre 2022

Introduzione
"Sonno e cognitività"

Marco Trabucchi
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Gruppo di ricerca geriatrica

ASSOCIAZIONE ITALIANA PSICOGERIATRIA

Le demenze, e l'Alzheimer in particolare, sono caratterizzate dalla complessità degli eventi, sia sul piano patogenetico (rapporto genetica-ambiente) sia sul piano fenomenologico.
Qualsiasi collegamento diretto con le dinamiche cliniche diventa quindi sempre difficile, come avviene nel caso del rapporto con il sonno.

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By Katharine Lang on June 13, 2022 — Fact checked by Alexandra Sanfins, Ph.D.

MEDICALNEWSTODAY

Dementia and sleep: What do we know about this link?

Dementia affects at least 55 million people worldwide and the number is increasing by about 10 million every year. In part, this is because we are living longer, but dementia is not an inevitable part of aging. So, are there ways to decrease our risk of developing dementia? Much research is currently focusing on the potential role of sleep.

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Gli studi sul rapporto sonno demenza sono numerosi.
Pubmed riporta 5611 citazioni su Sleep and Dementia.
Non sembra però un argomento maturo; ancora troppi punti oscuri.

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Gli aspetti principali sui quali è necessario concentrare gli studi e le ricerche:

- Lack of sleep in middle age may increase dementia risk
- Association of sleep duration in middle and old age with incidence of dementia
- Do people with dementia sleep a lot during the day
- Management of insomnia in Alzheimer
- Sleep problems and caregiving

ARTICLE

https://doi.org/10.1038/s41467-021-22354-2 OPEN

nature COMMUNICATIONS

Association of sleep duration in middle and old age with incidence of dementia

Séverine Sabia[1,2]✉, Aurore Fayosse[1], Julien Dumurgier[1,3], Vincent T. van Hees[4], Claire Paquet[3], Andrew Sommerlad[5,6], Mika Kivimäki[2,7], Aline Dugravot[1] & Archana Singh-Manoux[1,2]

Sleep dysregulation is a feature of dementia but it remains unclear whether sleep duration prior to old age is associated with dementia incidence. Using data from 7959 participants of the Whitehall II study, we examined the association between sleep duration and incidence of dementia (521 diagnosed cases) using a 25-year follow-up. Here we report higher dementia risk associated with a sleep duration of six hours or less at age 50 and 60, compared with a normal (7 h) sleep duration, although this was imprecisely estimated for sleep duration at age 70 (hazard ratios (HR) 1.22 (95% confidence interval 1.01–1.48), 1.37 (1.10–1.72), and 1.24 (0.98–1.57), respectively). Persistent short sleep duration at age 50, 60, and 70 compared to persistent normal sleep duration was also associated with a 30% increased dementia risk independently of sociodemographic, behavioural, cardiometabolic, and mental health factors. These findings suggest that short sleep duration in midlife is associated with an increased risk of late-onset dementia.

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U.S. Department of Health & Human Services

NIH National Institutes of Health
Turning Discovery Into Health

April 27, 2021

Lack of sleep in middle age may increase dementia risk

- **People who slept six hours or less per night in their 50s and 60s were more likely to develop dementia later in life.**
- **The findings suggest that inadequate sleep duration could increase dementia risk and emphasize the importance of good sleep habits.**

Sadeghmousavi *et al. Journal of Neuroinflammation* (2020) 17:289
https://doi.org/10.1186/s12974-020-01960-9

Journal of Neuroinflammation

REVIEW Open Access

The effect of insomnia on development of Alzheimer's disease

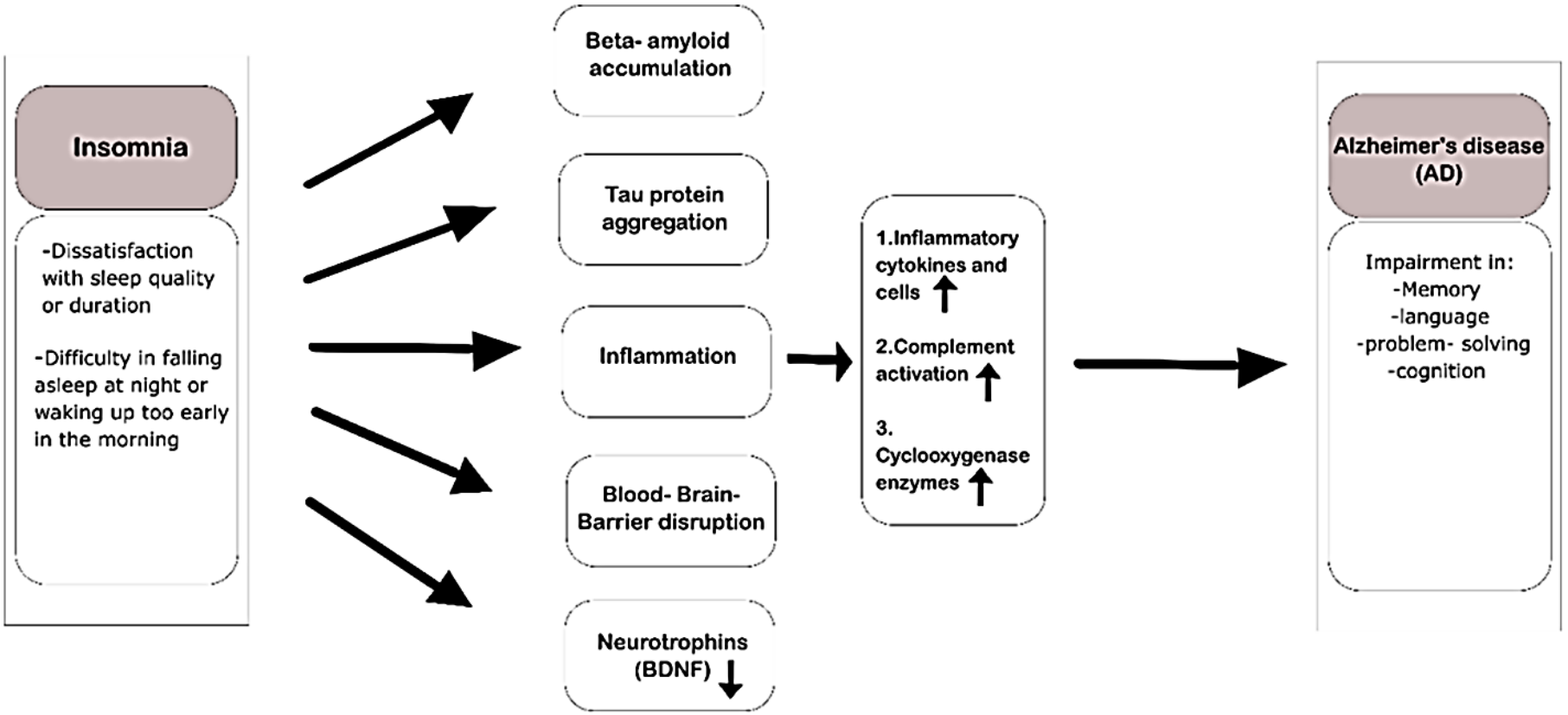
Shaghayegh Sadeghmousavi[1,2], Mahsa Eskian[1,3,4], Farzaneh Rahmani[1,3,5] and Nima Rezaei[1,3,4,6*]

Abstract

Alzheimer's disease (AD) is the most common type of dementia and a neurodegenerative disorder characterized by memory deficits especially forgetting recent information, recall ability impairment, and loss of time tracking, problem-solving, language, and recognition difficulties. AD is also a globally important health issue but despite all scientific efforts, the treatment of AD is still a challenge. Sleep has important roles in learning and memory consolidation. Studies have shown that sleep deprivation (SD) and insomnia are associated with the pathogenesis of Alzheimer's disease and may have an impact on the symptoms and development. Thus, sleep disorders have decisive effects on AD; this association deserves more attention in research, diagnostics, and treatment, and knowing this relation also can help to prevent AD through screening and proper management of sleep disorders. This study aimed to show the potential role of SD and insomnia in the pathogenesis and progression of AD.

Keywords: Alzheimer's disease, Sleep, Sleep deprivation, Insomnia, Inflammatory processes

The effect of insomnia on development of Alzheimer's disease



Sadeghmousavi *et al. Journal of Neuroinflammation* (2020) 17:289
https://doi.org/10.1186/s12974-020-01960-9

1. Induction of the extracellular release of tau which this increase can result in neurodegeneration and neuron loss and can explain the association of insomnia to AD pathogenesis.
2. Inflammation through increasing levels of proinflammatory cytokines and inflammatory agents and enzymes such as IL-6, TNF-α, and IL-1, and CRP and COX levels. However, the differences in the characterization of sleep disturbance, different assessment ways used to evaluate sleep disturbance such as sleep quality or other sleep complaints like sleep duration, and various markers of inflammation have led to not establishing confident results about the relation between sleep disturbances and inflammation.
3. The BBB disruption and 4. Declining in the neurotrophins levels which are essential proteins for neuron survival, modulation of neuronal function, and synaptic plasticity and have roles in neuroplasticity, memory, and sleep. Based on mentioned papers, these conditions due to insomnia can provide a basis for being affected by AD.

Sadeghmousavi *et al. Journal of Neuroinflammation* (2020) 17:289
https://doi.org/10.1186/s12974-020-01960-9

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… molte ipotesi, poche certezze

Identification and Management of Insomnia in Alzheimer's Disease

Thomas Roth, PhD; Stephen Brunton, MD, FAAFP

SUMMARY

Alzheimer's disease is an increasingly common, highly burdensome, and ultimately fatal disease. In addition to neuropsychiatric disorders, disruption of the sleep-wake cycle is common in people with AD, and may be caused by as well as contribute to AD itself. Assessing for the presence and consequences of insomnia and other sleep-related disorders is important. Little investigation in clinical trials has been undertaken to evaluate the safety and efficacy of medications for insomnia in people with AD, although the results of a trial of suvorexant in this setting have recently been reported at a national meeting but not yet published. The Beers Criteria for Potentially Inappropriate Medication Use in Older Adults recommends that many classes of medications used to treat insomnia not be used in older adults with dementia or cognitive impairment. These are first-generation antihistamines (including OTC sleep aids), some antidepressants, benzodiazepines, and "non-benzodiazepines." ●

J Fam Pract. 2019 Oct;68(8):S32-S38.

Questions should be asked to identify sleep patterns such as:

- When do you go to sleep?
- When do you arise?
- How many times a night do you awaken?
- When you awaken, how long does it take you to fall asleep?
- What percent of the time you spend in bed intending to sleep do you actually sleep?

In addition, questions should be asked about conditions that may make sleep problems worse, such as:

- Do you snore?
- Has anyone observed that you have episodes where you stop breathing?
- Do you feel a need to move your legs when at rest?
- Do you move around in bed a lot?
- Are you depressed?

J Fam Pract. 2019 Oct;68(8):S32-S38.

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Obstructive sleep apnea (OSA) occurs in half of patients with AD, with the OSA severity associated with dementia severity.

Restless leg syndrome is thought to occur in about 5% of patients with AD and can have a profound impact on sleep.

Depression occurs in up to 40% of people with AD, particularly in the early to middle stages of the disease.

J Fam Pract. 2019 Oct;68(8):S32-S38.

Review > J Alzheimers Dis. 2018;64(s1):S255-S270. doi: 10.3233/JAD-179936.

The Relationship between Obstructive Sleep Apnea and Alzheimer's Disease

Andreia G Andrade [1 2], Omonigho M Bubu [3], Andrew W Varga [4], Ricardo S Osorio [2 5]

Abstract

Go to:

Obstructive Sleep Apnea (OSA) and Alzheimer's disease (AD) are highly prevalent conditions with growing impact on our aging society. While the causes of OSA are now better characterized, the mechanisms underlying AD are still largely unknown, challenging the development of effective treatments. Cognitive impairment, especially affecting attention and executive functions, is a recognized clinical consequence of OSA. A deeper contribution of OSA to AD pathogenesis is now gaining support from several lines of research. OSA is intrinsically associated with disruptions of sleep architecture, intermittent hypoxia and oxidative stress, intrathoracic and hemodynamic changes as well as cardiovascular comorbidities. All of these could increase the risk for AD, rendering OSA as a potential modifiable target for AD prevention. Evidence supporting the relevance of each of these mechanisms for AD risk, as well as a possible effect of AD in OSA expression, will be explored in this review.

Keywords: Obstructive sleep apnea (OSA), Alzheimer's disease (AD), AD risk, OSA phenotypes, amyloid

Sleep. 2021 Sep 13;44(9):zsab076. doi: 10.1093/sleep/zsab076.

Obstructive sleep apnea treatment and dementia risk in older adults

Galit L Dunietz [1], Ronald D Chervin [1], James F Burke [2], Alan S Conceicao [2], Tiffany J Braley [1 3]

Abstract

Study objectives: To examine associations between positive airway pressure (PAP) therapy, adherence and incident diagnoses of Alzheimer's disease (AD), mild cognitive impairment (MCI), and dementia not otherwise specified (DNOS) in older adults.

Methods: This retrospective study utilized Medicare 5% fee-for-service claims data of 53,321 beneficiaries, aged 65 and older, with an obstructive sleep apnea (OSA) diagnosis prior to 2011. Study participants were evaluated using ICD-9 codes for neurocognitive syndromes (AD [n = 1,057], DNOS [n = 378], and MCI [n = 443]) that were newly identified between 2011 and 2013. PAP treatment was defined as the presence of at least one durable medical equipment (Healthcare Common Procedure Coding System [HCPCS]) code for PAP supplies. PAP adherence was defined as at least two HCPCS codes for PAP equipment, separated by at least 1 month. Logistic regression models, adjusted for demographic and health characteristics, were used to estimate associations between PAP treatment or adherence and new AD, DNOS, and MCI diagnoses.

Segue…

Sleep. 2021 Sep 13;44(9):zsab076. doi: 10.1093/sleep/zsab076.

Obstructive sleep apnea treatment and dementia risk in older adults

Galit L Dunietz [1], Ronald D Chervin [1], James F Burke [2], Alan S Conceicao [2], Tiffany J Braley [1 3]

Results: In this sample of Medicare beneficiaries with OSA, 59% were men, 90% were non-Hispanic whites and 62% were younger than 75 years. The majority (78%) of beneficiaries with OSA were prescribed PAP (treated), and 74% showed evidence of adherent PAP use. In adjusted models, PAP treatment was associated with lower odds of incident diagnoses of AD and DNOS (odds ratio [OR] = 0.78, 95% confidence interval [95% CI]: 0.69 to 0.89; and OR = 0.69, 95% CI: 0.55 to 0.85). Lower odds of MCI, approaching statistical significance, were also observed among PAP users (OR = 0.82, 95% CI: 0.66 to 1.02). PAP adherence was associated with lower odds of incident diagnoses of AD (OR = 0.65, 95% CI: 0.56 to 0.76).

Conclusions: PAP treatment and adherence are independently associated with lower odds of incident AD diagnoses in older adults. Results suggest that treatment of OSA may reduce the risk of subsequent dementia.

Keywords: Alzheimer's disease; CPAP; Medicare; mild cognitive impairment; obstructive sleep apnea.

Sleep. 2021 Sep 13;44(9):zsab076. doi: 10.1093/sleep/zsab076.

Obstructive sleep apnea treatment and dementia risk in older adults

Galit L Dunietz [1], Ronald D Chervin [1], James F Burke [2], Alan S Conceicao [2], Tiffany J Braley [1 3]

Statement of Significance

Emerging evidence has linked obstructive sleep apnea (OSA) to cognitive impairment and dementia incidence. However, research focused on the impact of OSA treatment on dementia is scarce. This analysis of Medicare Claims Data investigates associations between positive airway pressure (PAP) therapy and incident dementia diagnosis, at the population level. We demonstrate that treatment with PAP therapy was associated during a subsequent period of 3 years with lower odds of incident diagnoses of Alzheimer's dementia (AD) and dementia not otherwise specified. Adherence to PAP therapy was also associated with lower odds of incident AD diagnosis. These findings suggest a protective role of PAP therapy with respect to dementia among older adults with OSA.

BIOMOLECULES & THERAPEUTICS

Review
Biomol Ther 28(1), 58-73 (2020)

Impact of Sleep Disorder as a Risk Factor for Dementia in Men and Women

Hye Jin Jee[1,2], Wonseok Shin[1], Ho Joong Jung[1], Baekgyu Kim[3], Bo Kyung Lee[1] and Yi-Sook Jung[1,2,3,*]

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[3]Graduate School of Global Pharmaceutical Industry and Clinical Pharmacy, Ajou University, Suwon 16499, Republic of Korea

Abstract

Sleep is an essential physiological process, especially for proper brain function through the formation of new pathways and processing information and cognition. Therefore, when sleep is insufficient, this can result in pathophysiologic conditions. Sleep deficiency is a risk factor for various conditions, including dementia, diabetes, and obesity. Recent studies have shown that there are differences in the prevalence of sleep disorders between genders. Insomnia, the most common type of sleep disorder, has been reported to have a higher incidence in females than in males. However, sex/gender differences in other sleep disorder subtypes are not thoroughly understood. Currently, increasing evidence suggests that gender issues should be considered important when prescribing medicine. Therefore, an investigation of the gender-dependent differences in sleep disorders is required. In this review, we first describe sex/gender differences not only in the prevalence of sleep disorders by category but in the efficacy of sleep medications. In addition, we summarize sex/gender differences in the impact of sleep disorders on incident dementia. This may help understand gender-dependent pathogenesis of sleep disorders and develop therapeutic strategies in men and women.

Key Words: Sleep disorder, Therapeutics, Sex/gender differences, Dementia risk factor

Table 3. Sleep disturbance as a risk factor for dementia in men and women

Subtype of sleep disorder	Note	References
Insomnia	• Patients with primary insomnia had a higher risk of dementia incidence than those without insomnia. • Chronic insomnia increased the risk of incident cognitive decline in older men but not in order women. • Men with sleep disturbances had a higher risk of developing dementia and Alzheimer's disease.	Cricco *et al*., 2001 Shi *et al*., 2018 Benedict *et al*., 2015
Sleep-related breathing disorders (SRBD)	• Incident dementia is greater for patients with SA than those without SA. • Women with SA were more likely to develop dementia than men. • Old (≥65) women with SBD had a higher risk of developing cognitive impairment and dementia. • Men with sleep apnea had a higher risk of vascular dementia but not significant. • SA may be a risk factor for subcortical ischemic vascular dementia.	Chang *et al*., 2013 Yaffe *et al*., 2011 Elwood *et al*., 2011 Culebras and Anwar, 2018
Central disorders of hypersomnolence (CDH)	• EDS is a risk factor for dementia in men and women. • REM sleep behavior disorder patients with EDS had an increased risk of developing neurodegenerative diseases particularly PD but not dementia. • Men with daytime sleepiness had a higher risk of vascular dementia.	Jaussent *et al*., 2012 Zhou *et al*., 2017 Elwood *et al*., 2011
Circadian rhythm sleep-wake disorders (CRSD)	• Old (≥65) women with decreased circadian rhythm and delayed sleep phases were more likely to develop dementia. • Shorter time in bed (TIB) and later rise time increased the risk of incident dementia in men and women.	Tranah *et al*., 2011 Bokenberger *et al*., 2017
Parasomnias	• Shorter REM sleep percentage and longer latency to REM sleep were both associated with a higher risk of incident dementia. • PD with REM sleep behavior disorder patients are more likely to be male than female. • The occurrence rate of dementia in the PD group with clinical RBD was significantly higher than that in the PD group with normal REM sleep.	Pase *et al*., 2017 Jacobs *et al*., 2016 Romenets *et al*., 2012 Nomura *et al*., 2013
Sleep-related movement disorders (SRMD)	• SRMD patients had a nearly 4 times higher risk of incident all-cause dementia compared with individuals without SRMD. • Female SRMD patients had greater risk to develop all-cause dementia than male. • Restless legs syndrome patients had a higher risk of vascular dementia but not significant.	Lin *et al*., 2015 Elwood *et al*., 2011

Biomol Ther 28(1), 58-73 (2020)

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Disturbi del sonno e delirium sono eventi frequenti e spesso associati.
Le alterazioni cognitive sono fattori predisponenti il delirium; è quindi possibile tracciare un legame tra i tre eventi.

Journal of Sleep Research

REVIEW PAPER | Open Access

Pharmacological and non-pharmacological interventions to enhance sleep in mild cognitive impairment and mild Alzheimer's disease: A systematic review

Jonathan Blackman, Marta Swirski, James Clynes, Sam Harding, Yue Leng, Elizabeth Coulthard

First published: 02 December 2020 | https://doi.org/10.1111/jsr.13229 | Citations: 10

Segue…

Abstract

Suboptimal sleep causes cognitive decline and probably accelerates Alzheimer's Disease (AD) progression. Several sleep interventions have been tested in established AD dementia cases. However early intervention is needed in the course of AD at Mild Cognitive Impairment (MCI) or mild dementia stages to help prevent decline and maintain good quality of life. This systematic review aims to summarize evidence on sleep interventions in MCI and mild AD dementia. Seven databases were systematically searched for interventional studies where ≥ 75% of participants met diagnostic criteria for MCI/mild AD dementia, with a control group and validated sleep outcome measures. Studies with a majority of participants diagnosed with Moderate to Severe AD were excluded. After removal of duplicates, 22,133 references were returned in two separate searches (August 2019 and September 2020). 325 full papers were reviewed with 18 retained. Included papers reported 16 separate studies, total sample (n = 1,056), mean age 73.5 years. 13 interventions were represented: Cognitive Behavioural Therapy – Insomnia (CBT-I), A Multi-Component Group Based Therapy, A Structured Limbs Exercise Programme, Aromatherapy, Phase Locked Loop Acoustic Stimulation, Transcranial Stimulation, Suvorexant, Melatonin, Donepezil, Galantamine, Rivastigmine, Tetrahydroaminoacridine and Continuous Positive Airway Pressure (CPAP).

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REVIEW PAPER | Open Access

Pharmacological and non-pharmacological interventions to enhance sleep in mild cognitive impairment and mild Alzheimer's disease: A systematic review

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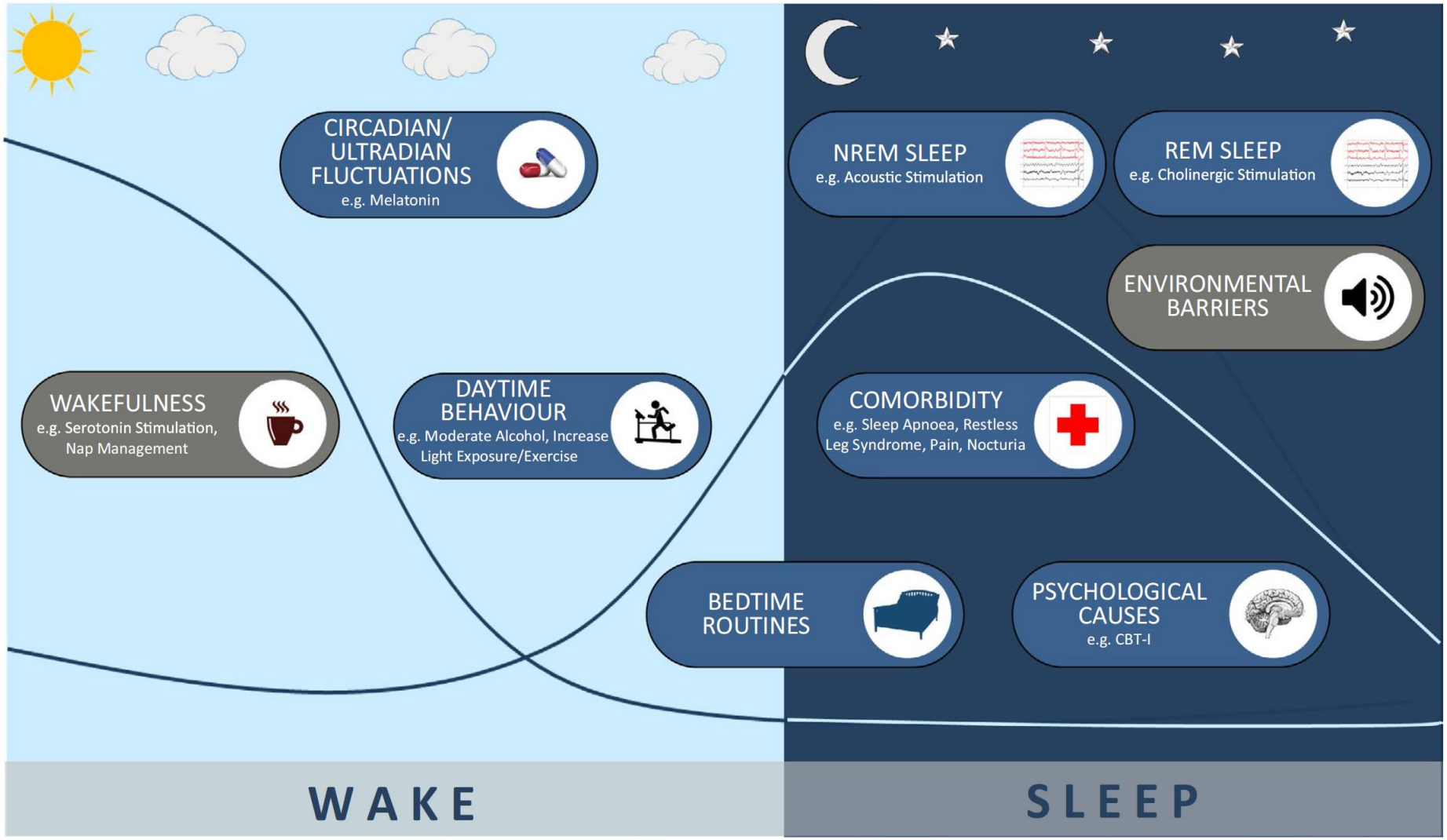
Psychotherapeutic approaches utilising adapted CBT-I and a Structured Limbs Exercise Programme each achieved statistically significant improvements in the Pittsburgh Sleep Quality Index with one study reporting co-existent improved actigraphy variables. Suvorexant significantly increased Total Sleep Time and Sleep Efficiency whilst reducing Wake After Sleep Onset time. Transcranial Stimulation enhanced cortical slow oscillations and spindle power during daytime naps. Melatonin significantly reduced sleep latency in two small studies and sleep to wakefulness transitions in a small sample. CPAP demonstrated efficacy in participants with Obstructive Sleep Apnoea. Evidence to support other interventions was limited. Whilst new evidence is emerging, there remains a paucity of evidence for sleep interventions in MCI and mild AD highlighting a pressing need for high quality experimental studies exploring alternative sleep interventions.

Theoretical interventional strategies to enhance sleep in people developing Alzheimer's disease



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Insonnia, demenza e aumento del burden fisico e psichico sui caregiver. Nelle fasi avanzate è il problema che grava più pesantemente sull'equilibrio delle famiglie.

Review > Sleep Med Rev. 2007 Apr;11(2):143-53. doi: 10.1016/j.smrv.2006.09.002.
Epub 2007 Feb 6.

Sleep disturbances in caregivers of persons with dementia: contributing factors and treatment implications

Susan M McCurry [1], Rebecca G Logsdon, Linda Teri, Michael V Vitiello

Abstract

Estimates suggest that there are more than 10 million adult caregivers of persons with dementia, two-thirds of who experience some form of sleep disturbance during the course of their caregiving career. Health care professionals are in the best position to detect and address this significant public health problem. Three major contributors to caregiver sleep disturbance are discussed in this paper: (1) the presence of caregiver disrupted sleep routines; (2) caregiver burden and depression; and, (3) the caregiver's physical health status. Successful treatment of a caregiver's sleep disturbance requires careful consideration of each of these contributors. We review and analyze the scientific literature concerning the multiple complex factors associated with the development and maintenance of sleep disturbances in caregivers. We provide a clinical vignette that illustrates the interplay of these contributing factors, and close by providing recommendations for clinicians and researchers treating and investigating the development and maintenance of sleep problems in family caregivers.

Review > Sleep Med Rev. 2007 Apr;11(2):143-53. doi: 10.1016/j.smrv.2006.09.002.
Epub 2007 Feb 6.

Sleep disturbances in caregivers of persons with dementia: contributing factors and treatment implications

Susan M McCurry [1], Rebecca G Logsdon, Linda Teri, Michael V Vitiello

Practice points

1. Since many caregivers are older adults, age-related changes in sleep architecture and circadian rhythmicity are important predisposing factors for caregiver subjective sleep complaints and a breakdown in optimal sleep habits and routines.
2. Nighttime awakenings by persons with dementia are a common precipitating cause of sleep/wake disturbances in vulnerable caregivers.
3. The development of poor sleep hygiene practices, sleep-wake scheduling irregularities, and decay of daytime structured social activities can perpetuate sleep disturbances and daytime fatigue in vulnerable caregivers.

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Aspetti da approfondire, attraverso ricerche e studi adeguati, sul rapporto sonno-demenze

- **Aspetti patogenetici**
- **La clinica**
- **Le possibili terapie farmacologiche (e non)**
- **L'evoluzione del deficit cognitivo**
- **Il peso sui caregiver**

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Nell'epoca della crisi dell'approccio farmacologico, l'identificazione dei fattori di rischio di demenza assume un ruolo strategico.

Allo stesso tempo, lo studio del sonno permette di impostare al meglio interventi che alleviano le difficoltà dell'assistenza alle persone affette da demenza.