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International Journal of Aging and Geriatric Medicine

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Vol: 1 & Iss: 1

Review

Geriatric Perspective: Sundown Syndrome and Dementia Diagnosis and Treatment

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Citation: Juri J. Geriatric Perspective: Sundown Syndrome and Dementia Diagnosis and Treatment. *Int J Aging Geriatr Med 2025*, 1(1), 34-39.

Received: 24 October, 2025; **Accepted:** 10 November, 2025; **Published:** 12 November, 2025

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1. Introduction

SUNDOWNING SYNDROME (or twilight syndrome) and dementia are conditions that frequently affect older adults, presenting significant challenges to diagnosis and treatment. A comprehensive geriatric perspective based on the current understanding of these conditions is offered below:

1.1. Symptoms

Sundowning syndrome is characterized by increased confusion, agitation, anxiety or disruptive behaviors in people with dementia, typically in the late afternoon or overnight. Symptoms include:

- **Agitation or restlessness:** Pacing, yelling or irritability.
- **Increased confusion:** Difficulty recognizing familiar people or places.
- **Sleep disturbances:** Insomnia or reversal of the sleep-wake cycle.
- **Delusions or hallucinations:** In some cases, misperceptions of reality.

1.2. Diagnostic methods

The diagnosis is mainly clinical, as there is no specific test for sundowning. Key steps include:

- **Detailed medical history:** Collect information from caregivers about the timing and nature of behaviors.
- **Cognitive and functional assessment:** Use tools such as the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA) to assess underlying dementia.
- **Rule out other causes:** Evaluate possible triggers such as:
  - Infections (e.g., UTI).
  - Untreated pain.
  - Medication side effects.
  - Metabolic disturbances (e.g., hypoglycemia, dehydration).
- **Temporal pattern observation:** Confirm whether symptoms intensify in the evening or overnight.

1.3. Treatment options

The management of sundowning combines non-pharmacological strategies and, in some cases, pharmacological interventions:

- **Non-pharmacological (first line):**
  - **Structured routines:** Maintain regular schedules for meals, activities and sleep.
  - **Optimizing the environment:** Reducing noise, providing adequate lighting during the day and decreasing excessive stimulation at night.
  - **Calming activities:** Soft music, aromatherapy or simple activities like folding laundry.

- **Daylight exposure:** Encourage morning walks or the use of phototherapy boxes to regulate the circadian rhythm.
- **Avoid triggers:** Limit caffeine, long naps and stressful events at the end of the day.

- **Pharmacological (only if necessary):**
  - Use with caution because of the risks in older adults.
  - **Melatonin:** May help regulate sleep, although evidence is mixed (dosage: 1-3 mg before bedtime).
  - **Antipsychotics (e.g., risperidone, quetiapine):** Reserved for severe cases with extreme agitation, in low doses and for a limited time due to the risk of adverse effects such as sedation or cardiovascular events.
  - **Cholinesterase inhibitors (e.g., donepezil):** These may be considered if the underlying dementia is Alzheimer's.
  - **Caregiver education:** Teach management strategies, communication techniques and the importance of their own well-being.

ALTHOUGH ITS PATHOPHYSIOLOGY is not fully elucidated due to its multifactorial nature and lack of specific studies, several mechanisms that interact with each other have been proposed. The main pathophysiological mechanisms involved are described below, based on the evidence available up to April 2025.

1.3.1. Circadian rhythm disturbances:

- **Description:** The biological clock, regulated by the suprachiasmatic nucleus (SCN) in the hypothalamus, controls circadian sleep-wake rhythms, body temperature and hormone release. In dementia, especially Alzheimer's disease (AD), the SCN has neuronal degeneration, which alters these rhythms.
- **Specific mechanisms:**
  - **SCN degeneration:** Post-mortem studies have shown neuronal loss and accumulation of amyloid plaques in the SCN in patients with AD, reducing its ability to synchronize circadian rhythms with the light-dark cycle.
  - **Melatonin disruption:** The production of melatonin, which regulates sleep, decreases with age and is aggravated in dementia. Nocturnal melatonin secretion is suppressed, contributing to insomnia and evening agitation.
  - **Environmental desynchronization:** Less exposure to daylight (due to institutionalization or reduced mobility) weakens the external signals (zeitgebers) necessary to maintain the circadian rhythm, exacerbating confusion at dusk[1].

1.3.2. Neurotransmitter dysfunction:

- **Description:** Alterations in neurotransmitter systems, such as cholinergic, serotonergic and dopaminergic, contribute to the behavioral and cognitive symptoms of sundowning.
- **Specific mechanisms:**
  - **Cholinergic deficiency:** In AD, the loss of cholinergic neurons in the basal Meynert nucleus and prefrontal cortex reduces the activity of acetylcholine, a key neurotransmitter for attention and memory. This deficiency can exacerbate confusion at the end of the day, when the cholinergic system is under greater stress.
  - **Serotonin disturbances:** The decrease in serotonin, seen in dementia, affects mood and sleep regulation. The drop in serotonin at the end of the day can contribute to the anxiety and agitation characteristic of sundowning.
  - **Dopaminergic dysregulation:** In dementias such as Lewy body dementia, dopaminergic fluctuations can cause hallucinations and evening agitation. The interaction between dopamine and melatonin can also destabilize the sleep-wake cycle[2].

1.3.3. Oxidative stress and neuroinflammation:

- **Description:** Neurodegeneration in dementia is associated with increased oxidative stress and chronic inflammation in the brain, which may amplify the symptoms of sundowning.
- **Specific mechanisms:**
  - **Accumulation of reactive oxygen species (ROS):** Oxidative damage in regions such as the hippocampus and prefrontal cortex affects emotional and cognitive regulation, increasing vulnerability to episodes of confusion at the end of the day.
  - **Microglial activation:** The release of pro-inflammatory cytokines (e.g., IL-6, TNF-α) by activated microglia contributes to synaptic dysfunction and may exacerbate agitation during times of fatigue or sensory overload.
  - **Interaction with circadian rhythms:** Inflammation alters the expression of clock genes (e.g., CLOCK, PER2), further desynchronizing the circadian rhythm[3].

1.3.4. Cognitive overload and fatigue:

- **Description:** Sundowning may be related to the accumulation of cognitive and physical fatigue throughout the day, which exceeds cognitive reserve capacity in patients with dementia.
- **Specific mechanisms:**
  - **Depletion of cognitive resources:** Daily cognitive demands (social interactions, activities) deplete executive functions, especially in the prefrontal cortex, resulting in emotional dysregulation at the end of the day.
  - **Hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis:** Accumulated stress activates the HPA axis, increasing evening cortisol levels, which can induce anxiety and confusion.
  - **Reduced cortical inhibition:** Fatigue decreases the ability of the prefrontal cortex to inhibit impulsive emotional responses, contributing to agitation[4].

1.3.5. Sensory and perceptual alterations

- **Description:** Visual and auditory deficits, common in older adults, can exacerbate confusion in low-light or high-stimulation settings at dusk.

- **Specific mechanisms:**
  - **Decreased visual acuity:** Reduced light at the end of the day makes it difficult to perceive the environment, increasing disorientation and anxiety.
  - **Impaired sensory processing:** In dementia, the processing of visual and auditory stimuli is compromised, which can lead to misinterpretations (e.g., shadows perceived as threats).
  - **Interaction with hallucinations:** In Lewy body dementia, alterations in the visual pathway (occipitoparietal cortex) can generate evening hallucinations, contributing to sundowning[5].

1.3.6. Systemic factors and comorbidities

- **Description:** Underlying medical conditions may interact with neurodegeneration to exacerbate sundowning.
- **Specific mechanisms:**
- **Untreated chronic pain:** Pain (e.g., from arthritis) may intensify at the end of the day, contributing to restlessness and agitation.
- **Infections or metabolic imbalances:** UTIs, hypoglycemia or dehydration can trigger or aggravate evening symptoms by disturbing the homeostatic balance.
- **Drug effects:** Some drugs (e.g., benzodiazepines, anticholinergics) alter alertness or sleep, increasing vulnerability to sundowning[6].

1.4. Interaction de mechanisms

El sundowning resulta de la convergencia de estos mecanismos en un contexto de vulnerabilidad cerebral. Por ejemplo:

- La degeneración del NSQ y la disminución de melatonina desregulan el sueño, lo que aumenta la fatiga cognitiva.
- La fatiga, combinada con déficits colinérgicos y sensoriales, reduce la capacidad de procesar estímulos ambientales, desencadenando ansiedad.
- La neuroinflamación y el estrés oxidativo amplifican la disfunción neuronal, mientras que comorbilidades sistémicas actúan como desencadenantes adicionales.
- Factores externos, como la disminución de luz o un entorno ruidoso, interactúan con estas alteraciones biológicas para precipitar los síntomas.

1.5. Limitations in knowledge

- **Lack of specific studies:** Most of the data comes from general dementia research, not studies designed for sundowning.
- **Clinical heterogeneity:** Symptoms vary between patients and types of dementia (Alzheimer's, Lewy bodies, vascular), complicating the identification of universal mechanisms.
- **Limited animal models:** Current models do not fully replicate sundowning, making experimental validation difficult.

1.6. Conclusion

Sundowning is the result of a complex interaction between circadian disturbances, neurochemical dysfunction, oxidative stress/inflammation, cognitive fatigue, sensory deficits and systemic comorbidities. Degeneration of the suprachiasmatic nucleus and cholinergic deficiency are central, but external factors and the progression of dementia modulate the expression of symptoms. Understanding these mechanisms allows for the design of targeted interventions, such as optimizing ambient light, pain management or cautious use of melatonin, although more research is needed to elucidate the specific pathways and develop more effective treatments **(Table 1)**.

Table 1: For Visual Representation.

Mechanism	Subcomponents	Contribution to Sundowning	Key Interactions
Circadian Rhythm Disturbances	SCN degeneration Melatonin decrease Light-dark desynchronization	Insomnia, evening confusion	Cognitive Fatigue, Neuroinflammation
Neurotransmitter Dysfunction	Cholinergic deficiency Serotonergic alterations Dopaminergic dysregulation	Confusion, agitation, hallucinations	Cognitive fatigue, sensory disturbances
Oxidative Stress and Neuroinflammation	ROS Citoquinas (IL-6, TNF- α) Microglial activation	Amplifies agitation and confusion	Circadian rhythm, neurotransmitter dysfunction
Cognitive Overload and Fatigue	Cognitive exhaustion Eje HHA (cortisol) Cortical inhibition reduction	Emotional dysregulation	Circadian rhythm, neurotransmitter dysfunction
Sensory and Perceptual Alterations	Decreased visual acuity Altered processing Hallucinations	Anxiety, disorientation	Neurotransmitter dysfunction, cognitive fatigue
Systemic Factors and Comorbidities	Chronic pain Infections Drug effects	Triggers or aggravates symptoms	Neuroinflammation, Cognitive Fatigue

1.7. Integrated geriatric perspective

- **Person-centred approach:** Tailoring interventions to the patient's needs, preferences and values.
- **Multidisciplinary team:** Involve geriatricians, neurologists, psychologists, occupational therapists and social workers.
- **Secondary prevention:** Identifying and treating factors that exacerbate symptoms, such as infections, malnutrition or polypharmacy.
- **Caregiver support:** Provide education, resources and strategies to reduce stress and prevent burnout.

2. Pharmacological Treatments for Sundowning Syndrome

Sundowning has no specific approved drug treatments, but some medications are used to manage symptoms such as agitation, anxiety or sleep disorders. Evidence is limited and non- pharmacological approaches are often prioritized. Relevant research is highlighted below[7]:

2.1. Melatonin for sleep disorders and sundowning

- **Design:** Systematic review of randomized controlled trials

(RCTs) evaluating melatonin in people with dementia and sleep disorders, including symptoms of sundowning.

- **Results:** Studies suggest that low doses of melatonin (1-3 mg before bedtime) may improve sleep quality and reduce nocturnal agitation in some patients with dementia. However, the effects are modest and not consistent across all participants. The combination with daylight exposure (phototherapy) showed additional benefits in some cases.
- **Limitations:** Heterogeneity in studies, small sample sizes and lack of standardized measures to assess sundowning specifically.
- **Bottom line:** Melatonin is a low-risk option, but the evidence is not robust enough to recommend it universally[8].

2.2. Antipsychotics for severe agitation

- Design: Multicenter clinical trial (CATIE-AD) evaluating atypical antipsychotics (risperidone, olanzapine, quetiapine) in patients with Alzheimer's and behavioral symptoms, including evening agitation.
- Results: Antipsychotics reduced agitation and psychotic symptoms in a subgroup of patients, but the benefits were modest and offset by adverse effects such as sedation, confusion and cardiovascular risk. Risperidone showed a slight advantage in controlling aggressiveness.
- Limitations: High risk of side effects, including increased mortality in older patients with dementia. Sundowning was not specifically studied as a primary variable.
- Bottom Line: Antipsychotics should be reserved for severe cases and used with extreme caution because of the risks[9].

2.3. Trazodone for insomnia and agitation

- **Design:** RCT evaluating trazodone (50-150 mg) versus placebo in patients with dementia and sleep disorders, some with symptoms of sundowning.
- **Results:** Trazodone improved sleep duration and quality, reducing nocturnal agitation compared to placebo. Side effects were minimal (mild daytime sleepiness).
- **Limitations:** Small sample size and lack of exclusive focus on sundowning. The results are not generalized to all types of dementia.
- **Bottom line:** Trazodone is a promising option for insomnia in dementia, with potential benefits in sundowning, but more studies are needed.

2.4. Conclusion

For sundowning syndrome, melatonin and trazodone show modest benefits in managing sleep and agitation, but antipsychotics should be used with caution because of their risks. In dementia, cholinesterase inhibitors and memantine are the most established treatments for AD and Lewy body dementia, while anti- amyloids emerge as promising but controversial options. Research highlights the need for comprehensive approaches that combine pharmacology with non- pharmacological strategies.

3. Non-Pharmacological Treatments for Sundowning Syndrome

3.1. Light therapy (Phototherapy)

- **Description:** Exposure to bright light, natural or artificial, during the day or at dusk seeks to regulate the circadian rhythm, improve sleep and reduce evening agitation by simulating sunlight.
- **Mechanism:** Bright light stimulates the suprachiasmatic nucleus, improving the synchronization of the sleep-wake cycle and increasing nocturnal melatonin production[10].
    - **Design:** Non-randomized controlled study with 70 dementia patients in nursing homes, exposed to bright light (2500 lux) for 1 hour daily (morning or afternoon) versus a control group.
    - **Results:** Morning exposure significantly reduced evening agitation and improved nighttime sleep consolidation compared to the control group. The effects were more pronounced in patients with moderate dementia.
    - **Limitations:** Lack of randomization and subjective measurement of agitation. Sundowning was not specifically assessed as a primary endpoint[11].
    - **Design:** Pilot study with 77 institutionalized patients, using bright light (2000-2500 lux) for 2 hours daily (morning or afternoon) for 10 weeks.
    - **Results:** Morning light improved nighttime sleep and reduced episodes of agitation at dusk in 20-30% of cases, as measured by actigraphy and behavioral scales.
    - **Limitations:** Small sample size and lack of a robust placebo group[12].
    - **Conclusion:** Although the evidence for phototherapy in sundowning is promising, there are no specific randomized controlled trials (RCTs). Open-label studies suggest benefits in agitation and sleep, but more research is needed.

3.2. Music therapy

- Description: Use of personalized, soft or familiar music (listening or actively participating) to reduce anxiety, agitation and improve the emotional state at sunset.
- Mechanism: Music stimulates brain areas related to emotional memory (e.g., amygdala, prefrontal cortex) and may decrease activation of the hypothalamic- pituitary-adrenal axis, reducing stress[13].
    - **Design:** RCT with 42 patients with moderate to severe dementia, assigned to individual music therapy sessions (30 min, 2 times per week) or standard care.
    - **Results:** Music therapy significantly reduced evening agitation (as measured by the Cohen-Mansfield Agitation Inventory) and improved mood in 60% of participants, especially with personalized music.
    - **Limitations:** Short duration of the study (6 weeks) and lack of long-term follow-up[14].
    - **Design:** Quasi-experimental study with 60 residents with dementia, using group music sessions (30 min, 2 times a week) for 6 weeks.
    - **Results:** The intervention decreased afternoon agitation and anxiety by 40%, with sustained effects for 2 weeks post-intervention.
    - **Limitations:** Absence of a randomized control group and dependence on subjective observations[15].

- **Design:** Observational study with 50 residents, using personalized playlists during the afternoon.
- **Results:** Music reduced disruptive behaviors by 35% during sundowning, with greater efficacy in patients with known musical preferences.
- **Limitations:** Uncontrolled design and lack of standardization in music selection.

3.3. Environmental modifications

- **Description:** Adjustments to the patient's environment, such as reducing noise, improving lighting, maintaining familiar objects and establishing consistent routines, to minimize confusion and anxiety.
- **Mechanism:** A predictable and calm environment reduces sensory overload and stress, facilitating temporal and spatial orientation[16].
  - **Design:** Quasi-experimental study with 66 patients in nursing homes, comparing warm (300-500 lux) versus standard (100 lux) ambient lighting during the afternoon.
  - **Results:** Warm lighting reduced evening agitation by 25% and improved social interaction, as measured by behavioral scales.
  - **Limitations:** Nonrandomized and moderate effects in severe dementia[17].
  - **Design:** Narrative review that includes studies on environmental modifications (e.g., noise reduction, structured routines).
  - **Results:** Consistent routines and minimization of stimuli (noise, sudden changes) decreased sundowning episodes by 20-40% in institutional settings.
  - **Limitations:** Lack of specific RCTs and heterogeneity in interventions[18].
  - **Design:** Systematic review of 33 studies on adapted environments.
  - **Results:** Interventions such as familiar objects, clear signage and noise reduction showed a significant decrease in evening agitation, although sundowning was not always specifically measured.
  - **Limitations:** Variability in designs and lack of exclusive focus on sundowning.

3.4. Physical activity and exercise

- **Description:** Activities such as walking, gentle exercise (e.g., tai chi) or structured programs during the day to improve sleep, reduce fatigue and stabilize mood.
- **Mechanism:** Exercise regulates the circadian rhythm, reduces cortisol and improves cerebral oxygenation, reducing agitation[19].
  - **Design:** Controlled study with 60 patients with AD, assigned to a daily walking program (30 min, 5 days/week) versus control.
  - **Results:** The exercise group showed a 30% reduction in sundowning symptoms (agitation, confusion) and lower levels of evening cortisol.
  - **Limitations:** Short duration (12 weeks) and lack of complete randomization[20].
  - **Design:** RCT with 96 patients, comparing morning walks (30 min, 5 days/week) versus standard care.
  - **Results:** Walking reduced nighttime restlessness and evening agitation by 25%, with improvements in sleep measured by actigraphy.
  - **Limitations:** Modest effects on severe dementia and variable adherence[21].
  - **Design:** RCT with 132 patients in community, using daily walks (30 min) for 6 months.
  - **Results:** The intervention decreased sundowning episodes by 20% and improved sleep quality, especially on morning walks.
  - **Limitations:** Reliance on caregivers for implementation.

3.5. Caregiver education and support

- Description: Programs to teach caregivers management strategies (e.g., calm communication, distraction, trigger management) and reduce caregiving stress.
- Mechanism: Improves patient-caregiver interaction, reduces conflicts and optimizes the environment, reducing the escalation of disruptive behaviors[22].
  - **Design:** RCT with 60 patient-caregiver dyads, using a training program (8 sessions) to identify triggers and personalize activities.
  - **Results:** Education reduced afternoon agitation by 35% and decreased caregiver stress, with sustained effects at 4 months.
  - **Limitations:** Requires time and resources for implementation[23].
  - **Design:** RCT with 153 patients, combining exercise and caregiver training (12 sessions).
  - **Results:** The combined intervention reduced disruptive behaviors (including sundowning) by 40% and improved physical function.
  - **Limitations:** Complexity of the intervention and need for committed caregivers[24].
  - **Design:** Pilot study with 30 caregivers, using 6-week workshops on sundowning management.
  - **Results:** Caregivers reported a 25% reduction in the frequency of evening episodes after learning distraction and relaxation techniques.
  - **Limitations:** Small sample size and uncontrolled design.

3.6. Other complementary therapies (aromatherapy, multisensory therapy)

- **Description:** Use of scents (e.g., lavender), multisensory stimulation (e.g., Snoezelen rooms) or calming activities (e.g., gentle massage) to reduce agitation.
- **Mechanism:** These therapies modulate emotional response, reduce stress and promote relaxation through non-invasive sensory stimuli[25].
  - **Design:** RCT with 15 patients with severe dementia, using lavender oil (diffuse aromatherapy) versus placebo for 2 weeks.
  - **Results:** Lavender reduced agitation in 60% of

cases, with noticeable effects at dusk, measured by behavioral scales.

- **Limitations:** Small sample size and short duration[26].
- **Design:** Pilot study with 36 patients, using essential oils (lavender, lemon) for 4 weeks.
- **Results:** Aromatherapy reduced evening agitation by 30% and improved mood, although the effects varied depending on the patient.
- **Limitations:** Lack of a robust control group and possible anosmia bias in dementia[27].
- **Design:** RCT with 50 patients, using multisensory sessions (light, sound, touch) versus standard activities.
- **Results:** Multisensory stimulation reduced anxiety and evening agitation by 25%, with greater engagement in patients with moderate dementia.
- **Limitations:** Effects not sustained after the cessation of the intervention.

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