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Review Article

Dual Orexin Receptor Antagonists for Nocturnal Agitation in Lewy Body Dementia: A Narrative Review and Clinical Trial Framework

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ABSTRACT

Nocturnal agitation in Lewy body dementia is a poorly defined syndrome arising from prolonged wakefulness, rapid eye movement sleep behavior disorder, hallucinations, cognitive fluctuation, pain, autonomic symptoms, sleep-disordered breathing, circadian disruption, medication effects, or superimposed delirium. This heterogeneity makes nonspecific sedation potentially hazardous. Dual orexin receptor antagonists reduce wake-promoting orexin signaling without directly enhancing gamma-aminobutyric acid transmission and therefore offer a biologically plausible treatment for an agitated-wake phenotype. This review evaluates the mechanistic rationale, clinical evidence, LBD-specific safety concerns, and trial-design requirements. Direct evidence is limited to a small uncontrolled study of lemborexant in 13 patients with dementia with Lewy bodies, which found no significant change in actigraphic sleep, rapid eye movement sleep behavior symptoms, or cognition. Randomized trials in Alzheimer dementia demonstrate that suvorexant can increase total sleep time and that lemborexant can improve selected rest-activity measures, but these findings do not establish efficacy for nocturnal agitation or safety in a synucleinopathy population. The principal risks in Lewy body dementia include next-day somnolence, falls, orthostatic symptoms, worsening cognitive fluctuation, hallucination-like experiences, and dream enactment. A definitive trial should enroll patients only after structured nocturnal phenotyping, use caregiver-verified minutes of agitated wakefulness corroborated by actigraphy as the primary endpoint, and require benefit without deterioration in prespecified neurological and functional safety

domains. Dual orexin receptor antagonists should currently be considered investigational for nocturnal agitation in Lewy body dementia, with future use guided by phenotype rather than by insomnia symptoms alone.

Categories: Neurology, Geriatrics, Therapeutics

Keywords: Lewy body dementia; Nocturnal agitation; Orexin antagonists; Insomnia; REM sleep behavior disorder; Actigraphy; Neuropsychiatric symptoms

INTRODUCTION

Lewy body dementia (LBD) includes dementia with Lewy bodies (DLB) and Parkinson disease dementia (PDD). The two diagnoses are separated clinically by the timing of dementia relative to parkinsonism, but both are synucleinopathies characterized by overlapping cognitive, neuropsychiatric, motor, autonomic, and sleep manifestations [1,2]. Treatment is unusually complex because cognitive fluctuation, recurrent visual hallucinations, parkinsonism, autonomic failure, and marked sensitivity to centrally acting medication may coexist in the same patient [1-3].

Nocturnal agitation is not a single sleep disorder. It is a practical clinical label for disruptive motor activity, calling out, wandering, fear, resistance to care, or aggression during the intended sleep period. Consensus descriptions of agitation emphasize excessive motor or verbal behavior associated with emotional distress, while classic dementia literature also recognizes that the same outward behavior may have different biological and environmental causes [4,5]. In LBD, the differential diagnosis includes sleep-maintenance insomnia, rapid eye movement (REM) sleep behavior disorder (RBD), hallucinations, delirium, pain, nocturia, constipation, orthostatic symptoms, sleep-disordered breathing, restless legs symptoms, medication effects, and circadian fragmentation.

Sleep disturbances are highly prevalent across the LBD spectrum and frequently overlap. Systematic and mechanistic reviews describe insomnia, excessive daytime sleepiness, RBD, fragmented sleep, sleep-disordered breathing, and impaired circadian organization [6,7]. Objective comparisons also suggest that DLB is associated with greater nocturnal movement and daytime sleepiness than Alzheimer disease [8]. These problems increase caregiver burden, worsen daytime function, and may accelerate institutional placement. Yet the evidence base for pharmacologic treatment remains limited, and a hypnotic that increases sleep duration may still be clinically unsuccessful if it leaves distressing agitation, dream enactment, falls, or caregiver disruption unchanged.

Dual orexin receptor antagonists (DORAs) suppress wake-promoting signaling through orexin-1 and orexin-2 receptors rather than producing broad gamma-aminobutyric acid-mediated inhibition. This mechanism has generated interest in dementia-related insomnia. The purpose of this narrative review is to assess whether DORAs have a credible role in LBD nocturnal agitation, distinguish the phenotype most likely to benefit, summarize direct and indirect clinical evidence, define LBD-specific risks, and propose a trial framework capable of producing clinically meaningful evidence.

REVIEW

Search strategy and scope

A focused narrative search of PubMed/MEDLINE and ClinicalTrials.gov was conducted through July 12, 2026. Search terms combined “Lewy body dementia,” “dementia with Lewy bodies,” “Parkinson disease dementia,”

"orexin," "suvorexant," "lemborexant," "daridorexant," "insomnia," "nocturnal agitation," and "REM sleep behavior disorder." Priority was given to diagnostic consensus statements, systematic reviews, randomized trials, and LBD-specific clinical studies. The aim was critical clinical synthesis and development of a testable trial framework. One small uncontrolled DLB study of lemborexant was identified, and no completed randomized trial specifically targeting nocturnal agitation in LBD was found.

Phenotyping nocturnal agitation

The first therapeutic decision is diagnostic rather than pharmacologic. Persistent wakefulness after sleep onset, accompanied by calling out, wandering, repeated reassurance seeking, or resistance to care, is the phenotype most directly aligned with orexin antagonism. By contrast, forceful limb movements, punching, kicking, or vocalization during vivid dreams suggest RBD; fearful interaction with formed images suggests hallucinations; and abrupt new nighttime disturbance should trigger evaluation for delirium, infection, pain, urinary retention, constipation, or medication toxicity. Table 1 summarizes a practical phenotype-first assessment.

Because patients with LBD often have impaired recall and fluctuating insight, caregiver observation is essential. A time-stamped event diary should document sleep opportunity, apparent wakefulness, the exact behavior, suspected triggers, caregiver intervention, and next-day consequences. Actigraphy can corroborate movement and rest-activity timing but cannot distinguish wakefulness from quiet hallucination or confirm REM sleep without atonia. Polysomnography is most valuable when RBD, sleep apnea, periodic limb movements, or diagnostically important nocturnal events remain uncertain.

Table 1: Phenotype-first assessment of nocturnal agitation in Lewy body dementia

Dominant phenotype	Clinical clues	Minimum confirmation	Implication for DORA use
Agitated wakefulness / sleep-maintenance insomnia	Long awake periods after sleep onset; calling out, wandering, repeated care seeking, or resistance	Time-stamped caregiver diary plus actigraphy; review sleep opportunity and daytime napping	Most biologically plausible target after reversible causes are addressed [4-8]
REM sleep behavior disorder	Dream enactment, punching, kicking, vocalization, or bed-partner injury; often later in the night	Collateral history and validated RBD screen; polysomnography when feasible	Not an insomnia surrogate; requires environmental safety and explicit stopping rules
Hallucinations or cognitive fluctuation	Fearful interaction with formed images or marked variation in attention and arousal	Neuropsychiatric assessment, fluctuation history, medication review, and delirium screen	Sedation may mask rather than treat the driver and can worsen daytime function
Medical or environmental trigger	Pain, nocturia, constipation, dyspnea, fever, urinary retention, or abrupt change from baseline	Focused examination and targeted investigation	Treat the trigger before any hypnotic trial
Circadian fragmentation	Frequent daytime sleep, weak day-night distinction, or prolonged evening inactivity	Seven- to 14-day rest-activity record and light/activity history	Prioritize circadian and behavioral intervention; drug effect may be nonspecific

DORA: dual orexin receptor antagonist; RBD: REM sleep behavior disorder.

Biological rationale for orexin antagonism

Orexin-A and orexin-B neurons in the lateral hypothalamus stabilize wakefulness and coordinate monoaminergic, cholinergic, autonomic, reward, and stress networks. DORAs reduce this wake drive through combined orexin-1 and orexin-2 receptor blockade. In a patient whose agitation is sustained by long nocturnal wake bouts, treatment could shorten wake after sleep onset, reduce opportunities for misperception or wandering, and decrease repeated caregiver intervention.

However, LBD does not appear to represent a simple state of orexin excess. Postmortem work has shown reduced hypocretin immunoreactivity in DLB, while cerebrospinal fluid studies have reported altered or subgroup-dependent orexin relationships [9,10]. Plasma orexin-A has been reported as elevated in prodromal LBD and associated with core clinical features, whereas cerebrospinal fluid orexin-A has correlated with RBD severity in DLB [11,12]. These apparently discordant observations may reflect regional neuronal loss, compensatory signaling, disease-stage effects, and unstable state regulation rather than a uniform directional abnormality. The translational implication is precision: orexin blockade may benefit persistent wakefulness but may worsen hypoarousal, daytime sleepiness, postural instability, or REM-related motor behavior. Figure 1 illustrates this phenotype-dependent model.

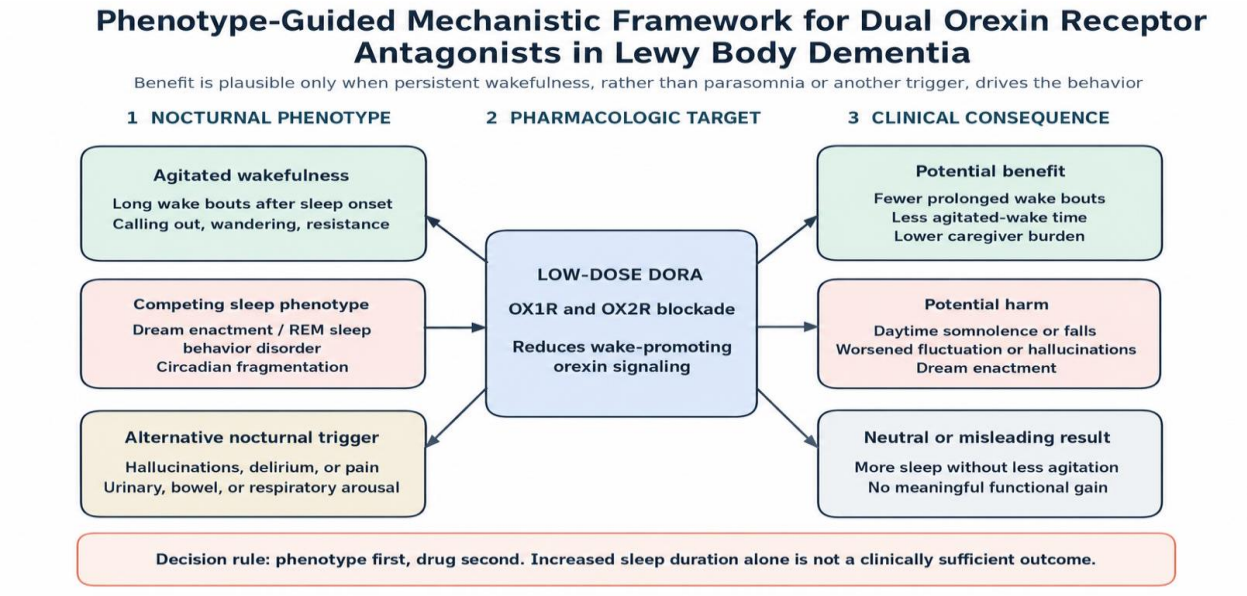

Figure 1: Phenotype-guided mechanistic framework. Orexin antagonism is most plausible when persistent wakefulness drives the behavior. The same intervention may be neutral or harmful when RBD, hallucinations, delirium, pain, or baseline hypoarousal predominates. Conceptual synthesis based on current LBD and orexin literature [1,3,6-12]. DORA: dual orexin receptor antagonist; LBD: Lewy body dementia; OX1R/OX2R: orexin-1/orexin-2 receptors; REM: rapid eye movement; RBD: REM sleep behavior disorder.

Current clinical evidence

The first direct clinical evidence in DLB was reported in 2026. Inagawa and colleagues administered lemborexant 5 mg to 13 patients with probable DLB and insomnia in a single-center before-and-after study [13]. Seven-day actigraphy and cognitive and sleep questionnaires showed no statistically significant changes in total sleep time, sleep efficiency, wake after sleep onset, number of awakenings, RBD screening score, or cognition. The absence of detected

deterioration is reassuring only in a limited sense. The study had no placebo group, was underpowered for modest benefit or uncommon harm, and used actigraphy, which cannot identify REM sleep without atonia. It therefore provides neither a reliable efficacy estimate nor definitive safety evidence for nocturnal agitation.

Indirect evidence comes primarily from Alzheimer dementia. In a four-week randomized trial of 285 participants with probable Alzheimer dementia and insomnia, suvorexant increased polysomnographic total sleep time by approximately 28 minutes more than placebo; somnolence occurred more often with active treatment [14]. In a phase 2 randomized dose-ranging trial involving 62 participants with Alzheimer dementia and irregular sleep-wake rhythm disorder, lemborexant improved selected actigraphic measures of nighttime rest and day-night rhythmicity without detected cognitive worsening [15]. These studies establish that orexin antagonism can modify sleep in dementia, but neither trial enrolled a representative synucleinopathy population or used nocturnal agitation as the primary clinical outcome.

In adults with insomnia, network meta-analysis supports short-term efficacy of DORAs for sleep initiation and maintenance [16]. Meta-analytic safety data identify somnolence and narcolepsy-like symptoms as class-relevant signals [17], while phase 3 daridorexant trials demonstrate improvement in nighttime sleep and daytime functioning in general insomnia populations [18]. Translation to LBD remains uncertain because patients with LBD are older, more likely to have autonomic dysfunction, gait impairment, cognitive fluctuation, hallucinations, RBD, and polypharmacy, and are commonly excluded from pivotal insomnia trials. Table 2 summarizes the evidence and its limitations.

Table 2: Clinical evidence relevant to dual orexin receptor antagonists in dementia and insomnia

Study	Population and design	Main finding	Interpretation for LBD nocturnal agitation
Inagawa et al., 2026 [13]	13 patients with probable DLB; lemborexant 5 mg; uncontrolled before-and-after study	No significant change in actigraphic sleep, RBD questionnaire score, or cognition	Direct but very low-certainty evidence; no efficacy estimate and inadequate power for uncommon harms
Herring et al., 2020 [14]	285 participants with probable Alzheimer dementia and insomnia; four-week randomized trial	Suvorexant increased total sleep time by about 28 minutes versus placebo; somnolence was more frequent	Supports sleep-maintenance efficacy in dementia, not agitation efficacy or LBD safety
Moline et al., 2021 [15]	62 participants with Alzheimer dementia and irregular sleep-wake rhythm; phase 2 dose-ranging trial	Lemborexant improved selected actigraphic rest-activity measures without detected cognitive worsening	Supports a circadian/sleep signal, but not transferability to synucleinopathy
General insomnia evidence [16-18]	Randomized trials and meta-analyses in adults with insomnia	Class efficacy for sleep initiation or maintenance; somnolence and narcolepsy-like symptoms remain relevant	Useful for mechanism and dose selection, but external validity to LBD is limited

DLB: dementia with Lewy bodies; LBD: Lewy body dementia; RBD: REM sleep behavior disorder.

Safety considerations and treatment context

The central safety question is whether reduced nighttime wakefulness is purchased at the cost of daytime dysfunction. Even mild residual sleepiness may worsen freezing, postural instability, orthostatic intolerance, attention, and dependence in activities of daily living. DORAs can also produce abnormal dreams, sleep paralysis, hallucination-like experiences, and complex sleep behaviors. A case report described suvorexant-associated dream enactment in Parkinson disease, highlighting a risk that is particularly relevant to synucleinopathy [19].

RBD requires explicit management rather than being treated as a surrogate for insomnia. Current clinical guidance prioritizes environmental safety, removal of dangerous objects, and individualized pharmacologic treatment when needed [20]. Excluding all patients with probable RBD would make an LBD trial poorly representative, but failing to stratify and monitor RBD would be unsafe. Baseline dream enactment frequency, bed-partner injury, bedroom safety, and rapid worsening after treatment should therefore be prespecified.

Before considering any hypnotic, clinicians should address reversible causes and optimize established LBD care. Medication review should identify anticholinergics, activating agents, evening dopaminergic dosing, sedative stacking, and drugs that worsen orthostasis. Evidence for pharmacologic management of LBD remains limited, and susceptibility to adverse effects is high [21]. Nonpharmacologic measures, including a stable sleep-wake schedule, daytime activity, reduction of excessive napping, environmental cues, and appropriately timed bright-light exposure, may improve rest-activity organization and behavior in dementia [22]. A DORA should not substitute for this assessment.

Proposed clinical trial framework

A clinically credible proof-of-concept study should be multicenter, randomized, double-blind, placebo-controlled, and short in duration. Eligible participants would have probable DLB or PDD, recurrent caregiver-observed nocturnal agitation on at least three nights per week, stable background medication, and a dominant agitated-wake phenotype after reversible causes are addressed. A 14-day run-in with actigraphy and an event diary would establish baseline frequency, confirm adequate sleep opportunity, and identify RBD, apnea, circadian reversal, pain, delirium, or medication-related disturbance.

Participants should be randomized 1:1 to one low-dose DORA or matched placebo for four weeks, with no forced titration. Randomization should be stratified by diagnosis, site, and probable RBD. The primary endpoint should be change in nightly minutes of caregiver-verified agitated wakefulness corroborated by actigraphy, rather than total sleep time alone. Actigraphy has demonstrated utility for tracking agitation-related activity and treatment response in dementia, although interpretation must remain linked to observed behavior [23]. Secondary outcomes should include wake after sleep onset, total sleep time, the Sleep Disorder Inventory, caregiver distress, global clinical change, and the Neuropsychiatric Inventory [24,25].

Efficacy must be coupled to a prespecified safety gate. A participant should be considered a responder only if agitated-wake time decreases by a clinically meaningful margin, such as at least 30%, without clinically important worsening in falls, orthostatic symptoms, daytime sleepiness, cognitive fluctuation, hallucinations, dream enactment, or treatment discontinuation. Figure 2 and Table 3 summarize the proposed design. This composite interpretation prevents a misleading conclusion in which improved sleep metrics obscure neurological or functional harm.

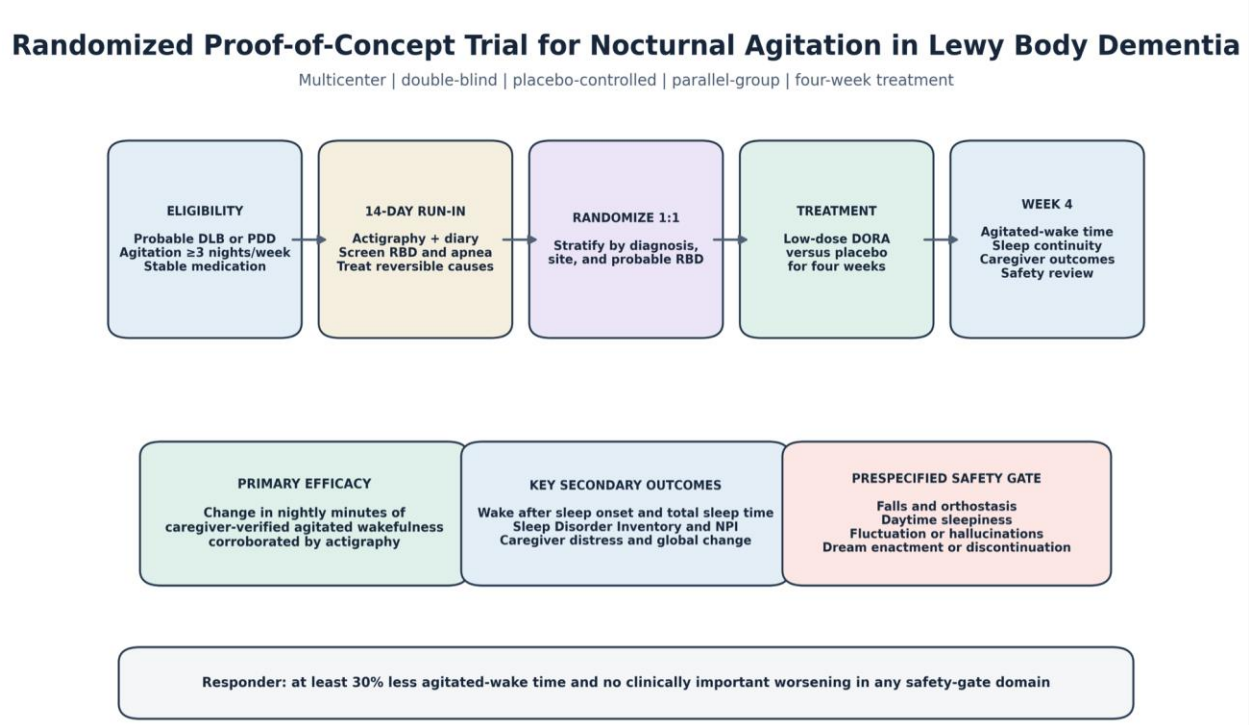

Figure 2: Proposed randomized proof-of-concept trial. The design prioritizes phenotype enrichment, a caregiver-verified behavioral endpoint, objective corroboration, and a prespecified neurological safety gate [13-15,23-25]. DLB: dementia with Lewy bodies; DORA: dual orexin receptor antagonist; NPI: Neuropsychiatric Inventory; PDD: Parkinson disease dementia; RBD: REM sleep behavior disorder.

Table 3: Recommended specifications for a proof-of-concept trial

Domain	Recommended specification	Rationale
Population	Probable DLB or PDD; recurrent caregiver-observed agitation during intended sleep; stable background medication	Enriches for the clinical problem while retaining the LBD spectrum
Run-in	Fourteen days of actigraphy and event diary plus structured sleep, medical, environmental, and medication phenotyping	Separates agitated wakefulness from RBD, delirium, pain, respiratory arousal, and circadian fragmentation
Intervention	One low-dose DORA versus matched placebo for four weeks; no forced titration	Limits exposure in a neurologically vulnerable population and preserves interpretability
Primary endpoint	Change in nightly minutes of caregiver-verified agitated wakefulness corroborated by actigraphy	Measures the behavior that matters rather than sleep duration alone [23]
Secondary endpoints	Wake after sleep onset, total sleep time, Sleep Disorder Inventory, caregiver distress, global change, and NPI	Captures sleep continuity, behavioral burden, and patient-caregiver relevance [24,25]
Safety gate	Falls, orthostasis, daytime sleepiness, fluctuation, hallucinations, dream enactment, and discontinuation	Requires benefit without neurological or functional cost
Responder definition	At least 30% reduction in agitated-wake time with no clinically important safety-gate worsening	Prevents improved sleep metrics from obscuring clinically meaningful harm

DLB: dementia with Lewy bodies; DORA: dual orexin receptor antagonist; LBD: Lewy body dementia; NPI: Neuropsychiatric Inventory; PDD: Parkinson disease dementia; RBD: REM sleep behavior disorder.

DISCUSSION

The current evidence supports biological plausibility but not clinical adoption. DORAs differ mechanistically from benzodiazepines and nonbenzodiazepine hypnotics, and their ability to reduce wake after sleep onset may be advantageous when prolonged wakefulness is the proximal driver of agitation. Nevertheless, the direct DLB evidence is limited to an uncontrolled sample of 13 patients with no significant efficacy signal [13]. Alzheimer dementia trials are informative about sleep physiology but cannot resolve the central LBD question: whether less wakefulness produces less distressing behavior without worsening daytime alertness, gait, hallucinations, fluctuation, or RBD [14,15].

The term "nocturnal agitation" itself creates a major methodological challenge. It can aggregate several conditions with opposing treatment requirements. Orexin antagonism may be rational for agitated wakefulness, neutral for a behavior driven by pain or nocturia, and potentially harmful when dream enactment or baseline hypoarousal predominates. Phenotype enrichment is therefore not an optional refinement; it is necessary to avoid a false-negative trial caused by mechanistic heterogeneity and a false-positive trial driven by sleep duration rather than meaningful clinical benefit.

The proposed outcome strategy also addresses the limitations of conventional sleep endpoints. Polysomnography and actigraphy can quantify sleep continuity, but they do not fully capture fear, resistance, caregiver disruption, injury risk, or the functional consequences of next-day sedation. A caregiver-verified behavioral endpoint, objectively corroborated where possible and paired with a neurological safety gate, is more aligned with the treatment goal. Such an endpoint will require validation, standardized caregiver training, and blinded adjudication of ambiguous events.

This review has limitations. The search was narrative rather than systematic, the direct LBD literature is extremely small, and no head-to-head data identify the optimal DORA, dose, or treatment duration. Pharmacokinetic differences among suvorexant, lemborexant, and daridorexant may matter in an older population with frailty and polypharmacy, but comparative inference is premature. The proposed 30% responder threshold is clinically intuitive rather than validated. Future research should first establish feasibility, event classification reliability, and short-term safety before attempting larger comparative-effectiveness or pragmatic trials.

CONCLUSIONS

Dual orexin receptor antagonists are credible candidates for a narrowly defined agitated-wake phenotype in Lewy body dementia, but the available evidence is insufficient to support routine treatment of nocturnal agitation. The outward behavior must first be separated from rapid eye movement sleep behavior disorder, hallucinations, delirium, pain, autonomic symptoms, respiratory arousal, medication effects, and circadian disruption.

The next step should be a short, low-dose, placebo-controlled trial built around structured phenotyping and a safety-gated behavioral outcome. A clinically meaningful positive result must demonstrate less caregiver-verified agitated wakefulness without worsening alertness, falls, orthostasis, cognitive fluctuation, hallucinations, dream enactment, or daily function. Until such evidence is available, use should remain individualized, cautious, and explicitly experimental.

REFERENCES

1. McKeith IG, Boeve BF, Dickson DW, et al.: Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium. Neurology. 2017, 89:88-100. 10.1212/WNL.0000000000004058
2. Emre M, Aarsland D, Brown R, et al.: Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord. 2007, 22:1689-1707. 10.1002/mds.21507
3. Taylor JP, McKeith IG, Burn DJ, et al.: New evidence on the management of Lewy body dementia. Lancet Neurol. 2020, 19:157-169. 10.1016/S1474-4422(19)30153-X
4. Cummings J, Mintzer J, Brodaty H, et al.: Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. Int Psychogeriatr. 2015, 27:7-17. 10.1017/S1041610214001963
5. Cohen-Mansfield J, Billig N: Agitated behaviors in the elderly. I. A conceptual review. J Am Geriatr Soc. 1986, 34:711-721. 10.1111/j.1532-5415.1986.tb04302.x
6. Elder GJ, Lazar AS, Alfonso-Miller P, Taylor JP: Sleep disturbances in Lewy body dementia: a systematic review. Int J Geriatr Psychiatry. 2022, 37:1-22. 10.1002/gps.5814
7. Townsend LTJ, Anderson KN, Boeve BF, et al.: Sleep disorders in Lewy body dementia: mechanisms, clinical relevance, and unanswered questions. Alzheimers Dement. 2023, 19:5264-5283. 10.1002/alz.13350
8. Cagnin A, Fragiacomo F, Camporese G, et al.: Sleep-wake profile in dementia with Lewy bodies, Alzheimer's disease, and normal aging. J Alzheimers Dis. 2017, 55:1529-1536. 10.3233/JAD-160385
9. Lessig S, Ubhi K, Galasko D, et al.: Reduced hypocretin (orexin) levels in dementia with Lewy bodies. Neuroreport. 2010, 21:756-760. 10.1097/WNR.0b013e32833bfb7c
10. Wennstrom M, Londos E, Minthon L, Nielsen HM: Altered cerebrospinal fluid orexin and alpha-synuclein levels in dementia patients. J Alzheimers Dis. 2012, 29:125-132. 10.3233/JAD-2012-111655
11. Gan J, Liu S, Chen Z, et al.: Elevated plasma orexin-A levels in prodromal dementia with Lewy bodies. J Alzheimers Dis. 2022, 88:1037-1048. 10.3233/JAD-220082
12. Inagawa Y, Shimizu S, Takenoshita N, et al.: Association between cerebrospinal fluid orexin A level and severity of rapid eye movement sleep behavior disorder in dementia with Lewy bodies. Psychogeriatrics. 2021, 21:128-130. 10.1111/psyg.12618
13. Inagawa S, Yamamoto R, Inagawa Y, et al.: Tolerability of lemborexant for cognitive function and sleep quality in patients with dementia with Lewy bodies. J Alzheimers Dis Rep. 2026, 10:25424823261445626. 10.1177/25424823261445626
14. Herring WJ, Ceesay P, Snyder E, et al.: Polysomnographic assessment of suvorexant in patients with probable Alzheimer's disease dementia and insomnia: a randomized trial. Alzheimers Dement. 2020, 16:541-551. 10.1002/alz.12035
15. Moline M, Thein S, Bsharat M, et al.: Safety and efficacy of lemborexant in patients with irregular sleep-wake rhythm disorder and Alzheimer's disease dementia: results from a phase 2 randomized clinical trial. J Prev Alzheimers Dis. 2021, 8:7-18. 10.14283/jpad.2020.69

16. De Crescenzo F, D'Alo GL, Ostinelli EG, et al.: Comparative effects of pharmacological interventions for the acute and long-term management of insomnia disorder in adults: a systematic review and network meta-analysis. Lancet. 2022, 400:170-184. 10.1016/S0140-6736(22)00878-9
17. Na HJ, Jeon N, Staatz CE, et al.: Clinical safety and narcolepsy-like symptoms of dual orexin receptor antagonists in patients with insomnia: a systematic review and meta-analysis. Sleep. 2024, 47:zsad293. 10.1093/sleep/zsad293
18. Mignot E, Mayleben D, Fietze I, et al.: Safety and efficacy of daridorexant in patients with insomnia disorder: results from two multicenter, randomized, double-blind, placebo-controlled, phase 3 trials. Lancet Neurol. 2022, 21:125-139. 10.1016/S1474-4422(21)00436-1
19. Tabata H, Kuriyama A, Yamao F, et al.: Suvorexant-induced dream enactment behavior in Parkinson disease: a case report. J Clin Sleep Med. 2017, 13:759-760. 10.5664/jcsm.6600
20. Howell M, Avidan AY, Foldvary-Schaefer N, et al.: Management of REM sleep behavior disorder: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2023, 19:759-768. 10.5664/jcsm.10424
21. Stinton C, McKeith I, Taylor JP, et al.: Pharmacological management of Lewy body dementia: a systematic review and meta-analysis. Am J Psychiatry. 2015, 172:731-742. 10.1176/appi.ajp.2015.14121582
22. Figueiro MG, Sahin L, Kalsher M, et al.: Long-term, all-day exposure to circadian-effective light improves sleep, mood, and behavior in persons with dementia. J Alzheimers Dis Rep. 2020, 4:297-312. 10.3233/ADR-200212
23. Mahlberg R, Walther S: Actigraphy in agitated patients with dementia: monitoring treatment outcomes. Z Gerontol Geriatr. 2007, 40:178-184. 10.1007/s00391-007-0420-z
24. Hjetland GJ, Nordhus IH, Pallesen S, et al.: An actigraphy-based validation study of the Sleep Disorder Inventory in the nursing home. Front Psychiatry. 2020, 11:173. 10.3389/fpsyt.2020.00173
25. Cummings JL, Mega M, Gray K, et al.: The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology. 1994, 44:2308-2314. 10.1212/WNL.44.12.2308.