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Recent Advances in Drug-Related REM Sleep Behavior Disorder: A Postprint

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Abstract

REM sleep behavior disorder (RBD) is a parasomnia characterized primarily by loss of muscle atonia and dream enactment behaviors during REM sleep, often causing significant impairment to the quality of life of patients and their bed partners. Based on the presence or absence of clear precipitating factors for RBD, it can be classified into idiopathic RBD and secondary RBD, the latter of which is frequently associated with narcolepsy, autoimmune and inflammatory diseases, and medication use. In recent years, case reports have successively documented that antidepressants, antipsychotics, and several other drugs can induce or exacerbate drug-related RBD. Therefore, this article primarily conducts a systematic review of drug-related RBD and summarizes its pathophysiological mechanisms and treatment approaches.

Full Text

Recent Advances in Drug-Related Rapid Eye Movement Sleep Behavior Disorder Research

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Abstract

Rapid eye movement sleep behavior disorder (RBD) is a parasomnia characterized by the loss of muscle atonia and the enactment of dreams during REM

sleep, which can significantly impact the quality of life for both patients and their bed partners. RBD can be classified into two types based on the presence or absence of clear precipitating factors: idiopathic rapid eye movement sleep behavior disorder (iRBD) and secondary rapid eye movement sleep behavior disorder (sRBD). The latter is often associated with conditions such as narcolepsy, autoimmune and inflammatory diseases, and medication use. In recent years, there have been increasing case reports that antidepressants, antipsychotics, and other medications can induce or exacerbate drug-related RBD. This article provides a systematic review of drug-related RBD, summarizing its pathological mechanisms and treatment approaches.

Keywords: REM sleep behavior disorder; Drug; REM sleep; Review

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Rapid eye movement sleep behavior disorder (RBD) is defined by the presence of REM sleep without atonia (RSWA) and dream enactment behavior (DEB) during REM sleep, manifesting primarily as unpleasant dreams accompanied by violent behaviors related to dream content, such as punching, jumping out of bed, and shouting. These behaviors not only severely disrupt sleep quality for patients and their bed partners but may also cause self-injury or harm to bed partners due to violent movements. Studies show that 48% to 77% of RBD patients or their bed partners have suffered injuries from these behaviors [1]. Based on the presence of identifiable causative factors, RBD can be divided into idiopathic RBD (iRBD) and secondary RBD (sRBD). The former often represents the prodromal stage of alpha-synucleinopathies, with research confirming that 70% to 80% of iRBD patients will develop neurodegenerative diseases within 15 years of onset [2]. The latter is frequently associated with narcolepsy, autoimmune and inflammatory diseases, and medication use. Notably, due to biopsychosocial and environmental influences, an increasing number of people suffer from anxiety and depression. Recent epidemiological surveys indicate that the prevalence of depressive disorders among Chinese adults has reached 6.8% [3], leading to more widespread clinical use of antidepressants. However, case reports have increasingly documented RBD emergence following antidepressant use. Additionally, some antipsychotics and other medications have been reported to cause similar adverse reactions, though the pathological mechanisms underlying this drug-related RBD remain unclear.

Moreover, because RBD itself has a low incidence rate—estimated at 3% to 10% globally using the REM Sleep Behavior Disorder Screening Questionnaire [1] and only 1% confirmed by overnight polysomnography (PSG) monitoring [4]—drug-related RBD is even rarer. Consequently, clinicians often struggle to associate these symptoms with medication use, resulting in most patients being misdiagnosed or missed entirely, thereby missing optimal treatment windows. To address these issues, we conducted a comprehensive search of CNKI, Wanfang Data, PubMed, and Web of Science databases from inception to March 2024. Chinese databases were searched using the terms "drug," "antidepressant," "antipsychotic," and "rapid eye movement sleep behavior disorder," while

English databases were searched using "drug," "antidepressant drugs," "antipsychotic drugs," and "rapid eye movement sleep behavior disorder." Inclusion criteria comprised literature on drug-related RBD, while exclusion criteria included irrelevant topics, low credibility, and unavailable full texts.

1. Pathogenesis of iRBD

In 1975, McCarley and colleagues [5] proposed the reciprocal interaction model of REM sleep, which posits that REM sleep initiation and termination are regulated by reciprocal interactions between brainstem neuronal systems: REM-on and REM-off. The REM-on system comprises cholinergic neurons in the laterodorsal tegmental nucleus (LDT) and pedunculopontine tegmental nucleus (PPT), glutamatergic neurons in the pontine reticular formation (PRF), and GABAergic neurons in the sublaterodorsal nucleus (SLD). The REM-off system consists of noradrenergic neurons in the locus coeruleus (LC), serotonergic neurons in the dorsal raphe nucleus (DRN), and GABAergic neurons in the lateral pontine tegmentum (LPT) and periaqueductal gray (PAG) [6]. REM sleep initiation begins when cholinergic neurons in the LDT/PPT stimulate glutamatergic neurons in the PRF, GABAergic neurons in the SLD, and activate themselves through positive feedback. Subsequently, activated cholinergic and SLD GABAergic neurons can inhibit REM-off cells in the LPT/PAG. The aminergic neurons in the LC/DRN can self-inhibit and are also inhibited by SLD GABAergic cells. This activation of the REM-on system and deactivation of the REM-off system allows REM sleep to initiate and maintain. However, as REM sleep progresses, cholinergic neurons activate aminergic neurons in the LC/DRN, enhancing their inhibition of LDT/PPT cholinergic neurons. Simultaneously, reduced inhibition of LPT/PAG by SLD GABAergic neurons gradually activates the REM-off system, terminating REM sleep [7].

In healthy individuals, muscles are generally atonic during REM sleep because REM-on activation drives postsynaptic excitation, promoting presynaptic glutamate release that activates GABA/glycinergic cells in the ventromedial medulla (VMM) to release inhibitory neurotransmitters to spinal anterior horn motor neurons, triggering muscle atonia. However, occasional muscle twitches may occur during REM sleep, possibly related to intermittent glutamate release mediated by the red nucleus terminal, but these twitches become abnormally increased in RBD [8]. Therefore, overactivation of the phasic motor pathway or damage to components of the muscle atonia pathway (such as cholinergic system degeneration, impaired SLD-to-VMM pathways, or pharmacological blockade of GABA/glycine receptors on spinal anterior horn motor neurons) can lead to RSWA during REM sleep.

Previous studies have confirmed overlapping pathophysiological mechanisms between depression and Parkinson' s disease (PD), with depressed patients having a 3.2-fold higher probability of developing PD than healthy individuals [9]. Kim et al. [10] also found that iRBD patients often experience depressive symptoms, with severity positively correlating with depression. Wang et al. [11] reported

that nearly 9% of patients with major depressive disorder in psychiatric outpatient clinics have comorbid RBD. Therefore, both depression and iRBD can serve as prodromal manifestations of PD, appearing independently or sequentially. However, it remains unclear whether antidepressant-related RBD is associated with synucleinopathy or represents a distinct form of RBD independent of synucleinopathy. Postuma [12] proposed three hypotheses: (1) Since both depression and iRBD are prodromal symptoms of PD, patients with depression who may develop PD already have underlying RBD risk factors, and antidepressants may trigger synucleinopathy-related subclinical RBD, though the probability of later PD conversion may be lower than in iRBD patients; (2) Antidepressants themselves do not induce RBD, and RBD appearing after medication use is merely a prodromal symptom of PD, with patients having both depression and iRBD potentially facing higher PD risk than those with iRBD alone; (3) Antidepressants independently induce a mechanistically distinct form of iRBD that may not progress to PD.

2. Pathogenesis of Drug-Related RBD

2.1 Antidepressants and RBD Based on mechanisms of action and chemical structure, antidepressants reported to cause RBD include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs).

2.1.1 SSRIs SSRIs are the most commonly used antidepressants, primarily inhibiting presynaptic reuptake of 5-HT to increase synaptic 5-HT levels and exert antidepressant effects [13]. However, as early as 1992, Schenck and colleagues reported RBD symptoms in a 31-year-old male with obsessive-compulsive disorder treated with fluoxetine 40 mg/d, with symptom resolution after drug discontinuation [14]. Subsequent case reports have documented sRBD in depressed patients using fluoxetine and paroxetine. These cases typically involve middle-aged men aged 30-50 who, despite remission of their primary condition, present with poor sleep quality or injury to bed partners due to nocturnal shouting and motor behaviors, with RBD symptoms gradually disappearing after drug cessation [15-16]. Additionally, Sheynter et al. [17] reported sRBD in an 87-year-old male treated with sertraline for post-traumatic stress disorder, with symptom disappearance after discontinuation. A subsequent prospective study investigating the association between sertraline and RSWA confirmed that sertraline can induce or worsen RSWA, with PSG showing that sertraline-related RSWA is associated with prolonged REM latency and is not predominantly male or elderly [18].

Interestingly, some SSRIs have shown protective effects and can alleviate RBD symptoms in iRBD patients. Two elderly women aged 72 experienced significant reductions in RBD episodes after treatment with paroxetine 10-20 mg/d, fluvoxamine 50 mg/night, and vortioxetine 10 mg/d [19-20]. The pathological

mechanism underlying this dual effect remains unclear, but current research suggests it may stem from different drug targets. When SSRIs bind to 5-HT1A receptors in the LDT/PPT, they can inhibit REM sleep and improve RBD; however, when binding to 5-HT1A receptors in the DRN, they reduce neuronal firing rates, disinhibiting LDT/PPT neurons and increasing REM sleep [20-21].

2.1.2 SNRIs SNRIs are dual-channel blockers that primarily inhibit presynaptic reuptake of both 5-HT and norepinephrine [22]. Previous case reports include an elderly female with somatoform disorder who developed abnormal nocturnal behaviors after taking duloxetine 60 mg/d. PSG monitoring at 7 and 31 months after medication initiation showed REM latency increased by 34.5 minutes, REM sleep time decreased by 82.5 minutes, and phasic and tonic electromyographic activity during REM increased by 32.5% and 7.6%, respectively. These RBD symptoms significantly improved 9 days after discontinuation and completely resolved after 37 days, with post-discontinuation PSG showing increased REM sleep time and significantly reduced phasic and tonic electromyographic activity [23]. Kluge et al. [24] also found in their study of depressed patients taking duloxetine that post-medication PSG showed significantly increased stage N3 sleep and REM latency, with reduced REM sleep time, indicating specific effects on sleep architecture. Venlafaxine has also been reported to cause RBD, with symptoms persisting for 13 years in a 55-year-old female taking venlafaxine 150 mg/d until gradual resolution after drug cessation [25]. The exact mechanism of SNRI-induced RBD remains unclear, but animal studies suggest it may result from increased norepinephrine in the synaptic cleft continuously activating LC REM-off cells, leading to REM sleep suppression, reduced inhibition of lower motor neurons, and RSWA. This persistent suppression may also create a state similar to REM sleep deprivation, increasing brain excitability and aggressive behaviors [26].

2.1.3 TCAs TCAs were once the primary treatment for depression and are also dual-channel blockers that inhibit reuptake of 5-HT and norepinephrine, increasing synaptic monoamine concentrations [27]. Beyond mood improvement, TCAs have been reported to treat cataplexy in narcolepsy patients [28-29]. However, case reports describe abnormal nocturnal behaviors in narcolepsy patients using clomipramine, with PSG showing significantly increased muscle tone during sleep that resolved after gradual dose reduction [30-31]. TCA-related RBD is thought to be associated with anticholinergic effects, though the exact mechanism requires further investigation [32].

2.1.4 MAOIs MAOIs are the earliest developed antidepressants, primarily preventing monoamine oxidase from clearing neurotransmitters like norepinephrine and 5-HT [33]. Previous case reports documented RSWA in four young males and three middle-aged females taking phenelzine 45-60 mg/d, and selegiline 5-10 mg/d was also found to cause RBD in elderly PD patients, with symptom resolution after discontinuation in all cases [34-35].

In summary, the temporal relationship between antidepressant use and RBD emergence, along with symptom and RSWA resolution after discontinuation, supports a causal association. Biscarini et al. [36] confirmed that although antidepressant-treated RBD patients have fewer neurodegeneration-related prodromal symptoms and lower risk than iRBD patients, relevant biomarkers persist. However, RBD symptoms typically rely on subjective reports from patients or families. When only RSWA exists or symptoms are mild without significant life impact, patients often do not seek medical attention. Therefore, antidepressants may merely exacerbate existing RBD symptoms, prompting medical consultation. During clinical evaluation, PSG only detects current abnormal EMG activity, and patients may incorrectly attribute RBD onset to medication while overlooking previous mild manifestations. This suggests that patients with depression who may develop PD already have underlying RBD risk factors, and antidepressants may trigger or worsen synucleinopathy-related subclinical RBD.

2.2 Atypical Antipsychotic-Related RBD Antipsychotics are classified as typical or atypical based on pharmacological action. Typical antipsychotics primarily block D2 receptors in the mesolimbic and mesocortical dopamine pathways with numerous adverse effects, while atypical agents exert effects through coordinated actions on noradrenergic and serotonergic systems [37]. Three case reports have suggested that quetiapine and olanzapine can cause RBD [38-40]. Compared with antidepressants, antipsychotic-related RBD has a more rapid onset without residual RSWA, typically emerging within days of medication initiation and resolving quickly after discontinuation, thus demonstrating a clearer temporal causal relationship.

2.3 Other Drug-Related RBD Beyond antidepressants and antipsychotics, other medications such as beta-blockers and cholinesterase inhibitors have been reported to induce or worsen RBD. Bisoprolol, a beta-blocker commonly used for hypertension, was previously reported to cause nightmares and other abnormal sleep behaviors, though without PSG evaluation [41-42]. Iranzo et al. [43] performed PSG monitoring in two hypertensive patients complaining of nocturnal abnormal behaviors, confirming that bisoprolol can induce RBD. Although symptoms resolved after discontinuation, RSWA persisted. Previous research has shown that norepinephrine around the locus coeruleus can stimulate medullary inhibitory magnocellular nuclei, causing hyperpolarization of spinal alpha motor neurons and muscle atonia. As a lipophilic drug that penetrates the blood-brain barrier, bisoprolol may block norepinephrine' s hyperpolarizing effects on motor neurons, thereby inducing RSWA. Early autopsy reports also demonstrated severe monoaminergic cell loss in the locus coeruleus region of RBD patients [43-45].

Cholinesterase inhibitors are first-line treatments for Alzheimer' s disease (AD). Similar to SSRIs, rivastigmine and donepezil have dual effects on RBD. They can induce reversible acute RBD in AD patients, an adverse effect that resolves

when dosing is changed from bedtime to morning or when clonazepam is administered at bedtime [46-47]. Conversely, they can also treat iRBD [48-49]. Staer et al. [50] found in a prospective study that iRBD patients in early disease stages experience significant progressive deterioration of brain cholinergic system function over three years. This acetylcholine reduction may weaken LDT/PPT stimulation of GABAergic neurons in the SLD, inhibiting presynaptic glutamate release and reducing inhibitory neurotransmitter quantity reaching spinal anterior horn motor neurons, leading to increased muscle tone. Therefore, cholinesterase inhibitors can supplement deficient acetylcholine and improve RBD symptoms.

3. Clinical Distinctions Between Drug-Related RBD and iRBD

Although drug-related RBD and iRBD share clinical features of nocturnal dream-associated shouting and punching/kicking, significant differences exist in other aspects. First, etiologically, drug-related RBD is clearly associated with medications, particularly antidepressants and antipsychotics, whereas iRBD patients often have no identifiable cause and typically present as a prodromal stage of neurodegenerative disease. Regarding typical patient populations, drug-related RBD occurs in individuals aged 29-88 years, mostly taking medications for psychiatric conditions (anxiety, depression, somatoform disorders, obsessive-compulsive disorder), while iRBD is common in people over 50 years with neurodegenerative disease risk and may progress to neurodegenerative disease within 15 years. Temporally, drug-related RBD onset varies by medication class: the temporal relationship is less clear with antidepressants, whereas antipsychotics like quetiapine can induce RBD within three days of initiation. On PSG monitoring, drug-related RBD shows not only increased phasic and tonic EMG activity during REM but also prolonged REM latency and shortened REM sleep time, though these REM sleep structural changes may be associated with antidepressant use itself rather than directly caused by drug-related RBD. Nevertheless, these PSG features can help differentiate drug-related RBD from iRBD. Finally, after discontinuation, antidepressant-related RBD symptoms and PSG-detected RSWA may gradually resolve over one week to two years, whereas antipsychotic-induced RBD symptoms typically disappear immediately after discontinuation without residual RSWA on REM-period PSG.

4. Treatment of Drug-Related RBD

Based on case reports, all patients experienced significant symptom relief after discontinuing the offending medication. Therefore, for RBD patients using high-risk drugs or those developing RBD after medication initiation, drug discontinuation should be considered based on clinical need and risk, with subsequent observation of symptom changes. Additionally, patients and caregivers should be advised to establish a safe sleep environment by removing sharp objects near the bed and adding guardrails and soft mattresses to prevent injury. When RBD is severe, placing pillows between the patient and bed partner or sleeping

separately is recommended to avoid accidental injury [51].

If non-pharmacological measures are difficult to implement or patients request medication, clonazepam and melatonin can be used as first-line treatments. However, due to the lack of large clinical trials, current recommendations are based primarily on clinical experience and observational studies [1]. Clinicians should be aware of associated risks when using these medications. For example, clonazepam' s main adverse effects include excessive sedation and cognitive impairment, requiring cautious use in patients with neurodegenerative diseases and obstructive sleep apnea. Melatonin is often used as an alternative for clonazepam-intolerant individuals, with previous studies demonstrating that 3-15 mg at bedtime can improve RBD symptoms. Common adverse effects include dizziness and sedation, which are typically mild. Other medications such as sodium oxybate, pramipexole, and rivastigmine have also been reported effective for RBD, though their mechanisms remain unclear [52-54]. Although current research hypothesizes that drug-induced RBD patients may face future risk of neurodegenerative disease development, evidence remains insufficient, particularly lacking large-scale, prospective long-term follow-up studies to clarify this association. Therefore, in clinical practice, whether to implement pharmacological intervention to prevent neurodegenerative disease development in these patients requires guidance from future in-depth and extensive research.

In summary, medications commonly causing drug-related RBD include antidepressants, atypical antipsychotics, and a few other drugs. Notably, although drug-induced RBD patients are generally younger and symptoms may gradually resolve after discontinuation, the relatively low incidence often prevents clinicians from associating symptoms with medication use. Therefore, future clinical practice should remind physicians to take comprehensive and detailed medical histories, emphasizing the impact of medications on sleep to better identify and manage RBD patients.

However, this study has limitations. First, given that the exact pathophysiological mechanisms between drugs and RBD remain unclear and research conclusions are primarily based on case reports lacking high-quality clinical studies, a definitive causal association cannot be established. Additionally, subjective reports from patients and families lack reliability, making it impossible to determine whether RBD symptoms emerging after medication use represent true drug induction or exacerbation of pre-existing symptoms. Therefore, future research should focus on the pathophysiological basis of drug-related RBD to clarify the drug-RBD association and guide rational clinical medication use.

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References

[1] SOBREIRA-NETO M A, STELZER F G, GITAÍ L L G, et al. REM sleep behavior disorder: update on diagnosis and management[J]. Arq Neuropsiquiatr, 2023, 81(12): 1179-1194. DOI: 10.1055/s-0043-1777111.

[2] POSTUMA R B, IRANZO A, HU M, et al. Risk and predictors of dementia and Parkinsonism in idiopathic REM sleep behaviour disorder: a multicentre study[J]. Brain, 2019, 142(3): 744-759. DOI: 10.1093/brain/awz030.

[3] LU J, XU X F, HUANG Y Q, et al. Prevalence of depressive disorders and treatment in China: a cross-sectional epidemiological study[J]. Lancet Psychiatry, 2021, 8(11): 981-990. DOI: 10.1016/S2215-0366(21)00251-0.

[4] HABA-RUBIO J, FRAUSCHER B, MARQUES-VIDAL P, et al. Prevalence and determinants of rapid eye movement sleep behavior disorder in the general population[J]. Sleep, 2018, 41(2): zsx197. DOI: 10.1093/sleep/zsx197.

[5] MCCARLEY R W, HOBSON J A. Neuronal excitability modulation over the sleep cycle: a structural and mathematical model[J]. Science, 1975, 189(4196): 58-60. DOI: 10.1126/science.1135627.

[6] HOLST S C, LANDOLT H P. Sleep-wake neurochemistry[J]. Sleep Med Clin, 2022, 17(2): 151-160. DOI: 10.1016/j.jsmc.2022.03.002.

[7] GOTT J A, STÜCKER S, KANSKE P, et al. Acetylcholine and metacognition during sleep[J]. Conscious Cogn, 2024, 117: 103608. DOI: 10.1016/j.concog.2023.103608.

[8] FRAIGNE J J, TORONTALI Z A, SNOW M B, et al. REM sleep at its core - circuits, neurotransmitters, and pathophysiology[J]. Front Neurol, 2015, 6: 123. DOI: 10.3389/fneur.2015.00123.

[9] SHEN C C, TSAI S J, PERNG C L, et al. Risk of parkinson disease after depression: a nationwide population-based study[J]. Neurology, 2013, 81(17): 1538-1544. DOI: 10.1212/WNL.0b013e3182a956ad.

[10] KIM H J, KIM S J, LEE S A. Severity of idiopathic rapid eye movement sleep behavior disorder correlates with depression and alexithymia[J]. Sleep Med, 2020, 74: 25-30. DOI: 10.1016/j.sleep.2020.05.039.

[11] WANG J, CHAU S W H, LAM S P, et al. Prevalence and correlates of REM sleep behaviour disorder in patients with major depressive disorder: a two-phase study[J]. J Neurol Neurosurg Psychiatry, 2022, 93(9): 1010-1017. DOI: 10.1136/jnnp-2022-328259.

[12] POSTUMA R B, GAGNON J F, TUINEAIG M, et al. Antidepressants and REM sleep behavior disorder: isolated side effect or neurodegenerative signal?[J]. Sleep, 2013, 36(11): 1579-1585. DOI: 10.5665/sleep.3102.

[13] LOCHMANN D, RICHARDSON T. Selective serotonin reuptake inhibitors[J]. Handb Exp Pharmacol, 2019, 250: 135-144. DOI: 10.1007/164_{{{2018}}}_{{172}}}.

[14] SCHENCK C H, MAHOWALD M W, KIM S W, et al. Prominent eye movements during NREM sleep and REM sleep behavior disorder associated with fluoxetine treatment of depression and obsessive-compulsive disorder[J]. Sleep, 1992, 15(3): 226-235. DOI: 10.1093/sleep/15.3.226.

[15] APPLEBEE G A, ATTARIAN H P, SCHENCK C H. An angry bed partner[J]. J Clin Sleep Med, 2009, 5(5): 477-479.

[16] PARISH J M. Violent dreaming and antidepressant drugs: or how paroxetine made me dream that I was fighting saddam hussein[J]. J Clin Sleep Med, 2007, 3(5): 529-531. DOI: 10.5664/jcsm.26919.

[17] SHEYNTER I, KHAN S, STEWART J T. A case of selective serotonin reuptake inhibitor-induced rapid eye movement behavior disorder[J]. J Am Geriatr Soc, 2010, 58(7): 1421-1422. DOI: 10.1111/j.1532-5415.2010.02947.x.

[18] ZHANG B, HAO Y L, JIA F J, et al. Sertraline and rapid eye movement sleep without Atonia: an 8-week, open-label study of depressed patients[J]. Prog Neuropsychopharmacol Biol Psychiatry, 2013, 47: 85-92. DOI: 10.1016/j.pnpbp.2013.08.010.

[19] DU Y L, JIANG J J, NG C H, et al. Vortioxetine improves rapid eye movement sleep behavior disorder: a case report[J]. J Clin Psychopharmacol, 2022, 42(5): 547-549. DOI: 10.1097/JCP.0000000000001605.

[20] TAKAHASHI T, MITSUYA H, MURATA T, et al. Opposite effects of SSRIs and tandospirone in the treatment of REM sleep behavior disorder[J]. Sleep Med, 2008, 9(3): 317-319. DOI: 10.1016/j.sleep.2007.05.003.

[21] HOPKINS S C, DEDIC N, KOBLAN K S. Effect of TAAR1/5-HT1A agonist SEP-363856 on REM sleep in humans[J]. Transl Psychiatry, 2021, 11(1): 228. DOI: 10.1038/s41398-021-01308-7.

[22] BONILLA-JAIME H, SÁNCHEZ-SALCEDO J A, ESTEVEZ-CABRERA M M, et al. Depression and pain: use of antidepressants[J]. Curr Neuropharmacol, 2022, 20(2): 384-402. DOI: 10.2174/1570159X19666210609161447.

[23] TAN L, ZHOU J Y, YANG L H, et al. Duloxetine-induced rapid eye movement sleep behavior disorder: a case report[J]. BMC Psychiatry, 2017, 17(1): 372. DOI: 10.1186/s12888-017-1551-0.

[24] KLUGE M, SCHÜSSLER P, STEIGER A. Duloxetine increases stage 3 sleep and suppresses rapid eye movement (REM) sleep in patients with major depression[J]. Eur Neuropsychopharmacol, 2007, 17(8): 527-531. DOI: 10.1016/j.euroneuro.2007.01.006.

[25] RYAN WILLIAMS R, SANDIGO G. Venlafaxine-induced REM sleep behavioral disorder presenting as two fractures[J]. Trauma Case Rep, 2017, 11: 18-19. DOI: 10.1016/j.tcr.2017.10.017.

[26] LEE K, BARON K, SOCA R, et al. The prevalence and characteristics of REM sleep without Atonia (RSWA) in patients taking antidepressants[J]. J

Clin Sleep Med, 2016, 12(3): 351-355. DOI: 10.5664/jcsm.5582.

[27] WATANABE K. Antidepressants[J]. Brain and Nerve, 2023, 75(5): 573-578. DOI: 10.11477/mf.1416202381.

[28] HISHIKAWA Y, IDA H, NAKAI K, et al. Treatment of narcolepsy with imipramine (tofranil) and desmethylimipramine (pertofran)[J]. J Neurol Sci, 1966, 3(5): 453-461. DOI: 10.1016/0022-510x(66)90001-3.

[29] ROTH B, FABER J, NEVSÍMALOVÁ S, et al. The influence of imipramine, dexphenmetrazine and amphetaminsulphate upon the clinical and polygraphic picture of narcolepsy-cataplexy[J]. Schweiz Arch Neurol Neurochir Psychiatr, 1971, 108(2): 219-228.

[30] ATTARIAN H P, SCHENCK C H, MAHOWALD M W. Presumed REM sleep behavior disorder arising from cataplexy and wakeful dreaming[J]. Sleep Med, 2000, 1(2): 131-133. DOI: 10.1016/s1389-9457(99)00013-1.

[31] GUILLEMINAULT C, RAYNAL D, TAKAHASHI S, et al. Evaluation of short-term and long-term treatment of the narcolepsy syndrome with clomipramine hydrochloride[J]. Acta Neurol Scand, 1976, 54(1): 71-87. DOI: 10.1111/j.1600-0404.1976.tb07621.x.

[32] ARNULF I. REM sleep behavior disorder: motor manifestations and pathophysiology[J]. Mov Disord, 2012, 27(6): 677-689. DOI: 10.1002/mds.24957.

[33] NAOI M, MARUYAMA W, SHAMOTO-NAGAI M. Neuroprotective function of rasagiline and selegiline, inhibitors of type B monoamine oxidase, and role of monoamine oxidases in synucleinopathies[J]. Int J Mol Sci, 2022, 23(19): 11059. DOI: 10.3390/ijms231911059.

[34] AKINDELE M O, EVANS J I, OSWALD I. Mono-amine oxidase inhibitors, sleep and mood[J]. Electroencephalogr Clin Neurophysiol, 1970, 29(1): 47-56. DOI: 10.1016/0013-4694(70)90127-3.

[35] LOUDEN M B, MOREHEAD M A, SCHMIDT H S. Activation by selegiline (Eldepryle) of REM sleep behavior disorder in Parkinsonism[J]. W V Med J, 1995, 91(3): 101.

[36] BISCARINI F, PIZZA F, VANDI S, et al. Biomarkers of neurodegeneration in isolated and antidepressant-related rapid eye movement sleep behavior disorder[J]. Eur J Neurol, 2024, 31(6): e16260. DOI: 10.1111/ene.16260.

[37] GRINCHII D, DREMENCOV E. Mechanism of action of atypical antipsychotic drugs in mood disorders[J]. Int J Mol Sci, 2020, 21(24): 9532. DOI: 10.3390/ijms21249532.

[38] TAN L, ZHOU J Y, LIANG B, et al. A case of quetiapine-induced rapid eye movement sleep behavior disorder[J]. Biol Psychiatry, 2014, 79(5): e11-e12. DOI: 10.1016/j.biopsych.2014.08.002.

[39] ZHAO H X, LI S, WANG Y M. A case report of atypical sleep in an ischemic stroke patient with psychiatric symptoms caused by olanzapine[J]. Front Neurol, 2023, 14: 1266204. DOI: 10.3389/fneur.2023.1266204.

[40] CHOW R T S, WHITING D, FAVRIL L, et al. An umbrella review of adverse effects associated with antipsychotic medications: the need for complementary study designs[J]. Neurosci Biobehav Rev, 2023, 155: 105454. DOI: 10.1016/j.neubiorev.2023.105454.

[41] KURIYAMA S. Bisoprolol-induced nightmares[J]. J Hum Hypertens, 1994, 8(9): 730.

[42] WESTERLUND A. Central nervous system side-effects with hydrophilic and lipophilic beta-blockers[J]. Eur J Clin Pharmacol, 1985, 28 Suppl: 73-76. DOI: 10.1007/BF00543714.

[43] IRANZO A, SANTAMARIA J. Bisoprolol-induced rapid eye movement sleep behavior disorder[J]. Am J Med, 1999, 107(4): 390-392. DOI: 10.1016/s0002-9343(99)00245-4.

[44] SIGAROUDI A, KINZIG M, WAHL O, et al. Quantification of bisoprolol and metoprolol in simultaneous human serum and cerebrospinal fluid samples[J]. Pharmacology, 2018, 101(1/2): 29-34. DOI: 10.1159/000480091.

[45] UCHIYAMA M, ISSE K, TANAKA K, et al. Incidental Lewy body disease in a patient with REM sleep behavior disorder[J]. Neurology, 1995, 45(4): 709-712. DOI: 10.1212/wnl.45.4.709.

[46] ROSS J S, SHUA-HAIM J R. Aricept-induced nightmares in Alzheimer' s disease: 2 case reports[J]. J Am Geriatr Soc, 1998, 46(1): 119-120. DOI: 10.1111/j.1532-5415.1998.tb01033.x.

[47] YEH S B, YEH P Y, SCHENCK C H. Rivastigmine-induced REM sleep behavior disorder (RBD) in a 88-year-old man with Alzheimer' s disease[J]. J Clin Sleep Med, 2010, 6(2): 192-194.

[48] RINGMAN J M, SIMMONS J H. Treatment of REM sleep behavior disorder with donepezil: a report of three cases[J]. Neurology, 2000, 55(6): 870-871. DOI: 10.1212/wnl.55.6.870.

[49] DI GIACOPO R, FASANO A, QUARANTA D, et al. Rivastigmine as alternative treatment for refractory REM behavior disorder in Parkinson' s disease[J]. Mov Disord, 2012, 27(4): 559-561. DOI: 10.1002/mds.24909.

[50] STAER K, IRANZO A, TERKELSEN M H, et al. Progression of brain cholinergic dysfunction in patients with isolated rapid eye movement sleep behavior disorder[J]. Eur J Neurol, 2024, 31(1): e16101. DOI: 10.1111/ene.16101.

[51] HOWELL M, AVIDAN A Y, FOLDVARY-SCHAEFER N, et al. Management of REM sleep behavior disorder: an American academy of sleep medicine systematic review, meta-analysis, and GRADE assessment[J]. J Clin Sleep Med, 2023, 19(4): 769-810. DOI: 10.5664/jcsm.10426.

[52] MOGHADAM K K, PIZZA F, PRIMAVERA A, et al. Sodium oxybate for idiopathic REM sleep behavior disorder: a report on two patients[J]. Sleep Med, 2017, 32: 16-21. DOI: 10.1016/j.sleep.2016.04.014.

[53] SASAI T, INOUE Y, MATSUURA M. Effectiveness of pramipexole, a dopamine agonist, on rapid eye movement sleep behavior disorder[J]. Tohoku J Exp Med, 2012, 226(3): 177-181. DOI: 10.1620/tjem.226.177.

[54] CHICA-URZOLA H L. Trazodone in REM sleep behavior disorder[J]. Rev Colomb Psiquiatr, 2015, 44(4): 251-255. DOI: 10.1016/j.rcp.2015.04.004.

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