Clonazepam and Other Therapies of RBD

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25.1 Introduction

RBD treatment should initially focus on controlling any sleep comorbidities (e.g., obstructive sleep apnea [OSA]), minimizing any offending medication, and maximizing the safety of the sleeping environment, as discussed by Howell in Chap. 23. The Standards of Practice Committee of the American Academy of Sleep Medicine has published a "best practice guide" for the treatment of RBD [1]. The quality and quantity of the published evidence were reviewed, and the Level A recommendation was to modify the sleep environment for patients with RBD who have sleep-related injury or in our opinion have the potential for sleep-related injury. Clonazepam and melatonin were the co-first-line medications in the Level B recommendation. Interestingly, in addition to human studies, clonazepam and melatonin were both demonstrated to be effective therapies in a transgenic mice model with deficient glycine and GABA transmission that recapitulated the cardinal features of RBD [2]. More than ten other medications were in the Level C list of alternative therapies. The worldwide clinical experience and the published evidence indicate that clonazepam and melatonin are clearly the predominant and most effective, sustained therapies of RBD. Melatonin therapy of RBD is discussed in Chap. 24. We will now focus on clonazepam therapy of RBD, followed by a review of Level C alternative pharmacotherapies and non-pharmacologic therapies. Table 25.1 contains the list of therapies for RBD.

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Table 25.1 Therapies of idiopathic and symptomatic RBD

Level A[a] secure the safety of the bedside environment
Level B[a] pharmacotherapy:
1. Clonazepam
2. Melatonin
Level C[a,b] pharmacotherapy:
3. Levodopa
4. Pramipexole
5. Rotigotine (transdermal patch)
6. Donepezil
7. Rivastigmine
8. Sodium oxybate
9. Clonidine
10. Desipramine
11. Imipramine
12. Paroxetine
13. Monoamine oxidase inhibitors
14. Carbamazepine
15. Zopiclone
16. Temazepam
17. Gabapentin
18. Cannabidiol
19. Yi-Gan San
Non-pharmacologic therapies:
1. Bed alarm
2. Immunosuppressive therapy (in CNS autoimmune diseases/paraneoplastic disorders)
3. Pallidotomy (in Parkinson's disease)
4. Bilateral subthalamic deep brain stimulation (in Parkinson's disease)

[a]From: Aurora RN, Zak RS, Maganti RK, et al.; Standards of Practice Committee; American Academy of Sleep Medicine. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med 2010;6(1):85–95

[b]Not all the medications listed in Level C were included in the above citation

25.2 Clonazepam therapy of RBD

Clonazepam, a potent benzodiazepine, was found to be effective in our index series of RBD patients at the Minnesota Regional Sleep Disorders Center [3, 4]. Clonazepam was chosen because many of the patients also had frequent periodic limb movements (PLMs) of NREM sleep, a polysomnographic (PSG) finding called "nocturnal myoclonus" in the 1980s. Case reports and case series in those years indicated that bedtime clonazepam was effective in controlling symptomatic "nocturnal myoclonus." After our initial REM-suppressing treatment strategy of RBD (with tricyclic antidepressants) failed due to intolerance, bedtime clonazepam

therapy was initiated, given its reported success with another motor disorder of sleep, viz., "nocturnal myoclonus" (PLMs) that also affected our RBD patients. We found that clonazepam not only rapidly controlled the problematic behaviors of RBD but also suppressed the disturbed dreaming (often involving aggressive confrontations) that is another hallmark of RBD. This linked benefit suggested a common pathophysiology for generating the disturbed dreaming and abnormal behaviors of RBD, consistent with involvement of brainstem motor pattern generators as encompassed by the "activation-synthesis" model of dream generation proposed by Hobson and McCarley [5].

The long half-life of clonazepam provides a greater degree of assurance to physicians and patients that it will still be bioactive during 8 h of sleep. This is of relevance as REM sleep, and thus the behaviors of RBD, predominates in the second half of the night. Conazepam does not suppress REM sleep motor tone but instead prevents the emergence of dream enactment behavior, through uncertain mechanisms.

Early large case series totaling >250 RBD patients reported a beneficial response rate to clonazepam therapy of up to 90% [6]. The world literature on clonazepam therapy of RBD, reported as small-to-large case series, now totals >500 cases, with >66% efficacy for full control of problematic RBD behaviors. The typical dose range is 0.25–1.0 mg at bedtime, ranging up to 2+ mg in select cases. Clonazepam is rarely associated with dosage tolerance (habituation effect), despite years of nightly therapy [7]. In the just-cited study, in 49 RBD patients receiving nightly clonazepam therapy for a mean 3.7 ± (SD) 2.3 years, there was no significant increase from the initial dose to the dose at the latest follow-up, 0.63 ± 0.4 mg vs. 0.97 ± 0.89 mg [7]. Also, side effects from clonazepam were uncommon (<10% of cases: morning sedation, memory dysfunction, alopecia, gastroesophageal reflux, erectile dysfunction, depression, and personality changes [emerging at the outset of therapy]), and there was no instance of misuse. As noted above, there is no published evidence that clonazepam restores normal REM atonia, and although there was initial preliminary evidence that it may reduce some of the excessive phasic EMG activity in REM sleep [8], a recent study did not confirm this finding [9].

The primary mechanism of action appears to be the control of the major, clinically problematic behaviors of RBD, without suppression of minor motor movements. This underscores the general clinical axiom that treatment should be focused primarily on the patient's chief complaint, which for RBD consists of controlling the injurious or potentially injurious behaviors, and not the minor movements. Nor is the restoration of REM atonia a necessary goal of treatment. The literature is devoid of any double-blind, placebo-controlled, randomized trials of clonazepam therapy of RBD [10–12]. However, given the recurrent injuries usually associated with RBD (with major morbidity and potential lethality [6, 13–15]), it is doubtful that an ethical treatment trial can be devised with the approval of an institutional review board. If such a trial could be devised and conducted in cases of milder RBD, i.e., not associated with violent behaviors, then the findings would not necessarily be considered generalizable to the more aggressive and violent cases of RBD.

Before initiating clonazepam therapy, any comorbid OSA should be either ruled out or else diagnosed and effectively controlled, and any offending medication (e.g. antidepressant) should be minimized or eliminated if appropriate to do so. Patients should be informed of possible side effects, as described above (along with dizziness and unsteadiness [16]). The treating physician should also be mindful of any emergent OSA triggered by clonazepam therapy of RBD [17]. Combined clonazepam-melatonin therapy can be effective in controlling RBD in patients who do not respond to either medication individually [16, 18, 19]. Furthermore, combination therapy can help facilitate lower doses of clonazepam that may minimize side effects.

Three recent studies on diverse aspects of clonazepam therapy of RBD will now be reviewed [9, 20, 21]. The first two studies were from the same center and assessed the long-term use of clonazepam in idiopathic RBD (iRBD) on REM and NREM sleep parameters and clinical treatment efficacy [9, 20]. In the first study of 57 consecutive iRBD patients (mean age, 69 years; 91% male), 42 iRBD patients not taking clonazepam (nor any other medicine) for RBD were compared with 15 iRBD patients taking clonazepam (0.5–1.0 mg) at bedtime [9]. The clonazepam-treated group had significantly lower amounts of sleep stage shifts, lower stage N1 sleep, lower % of wakefulness after sleep onset (WASO), and a higher sleep efficiency and stage N2 sleep%. None of the REM sleep parameters differed between the groups, including REM atonia index and number of REM phasic chin EMG activations. A subgroup of 13/15 clonazepam-treated iRBD patients was followed longitudinally, with vPSG parameters at a mean 2.5 year follow-up compared to the baseline parameters. These results again showed that clonazepam did not modify muscle tone during REM sleep in RBD. However, the CGI-S (clinical global impression-severity) scale scores improved with treatment. The conclusion was that clonazepam suppresses the major, clinically relevant, behavioral events in RBD and that this benefit may be related to the modification in dream content (which has been noted in numerous reports, beginning with the first formal reports on RBD [3, 4]).

The second study compared 15 patients with iRBD, 13 patients with narcolepsy-RBD, and 18 controls [20]. An additional measure that was quantified by automated analysis was NREM sleep instability. Patients with iRBD were reevaluated after a mean 2.8 years of nightly therapy with 0.5–1.0 mg clonazepam, which found increases in stages N2 and N3 sleep, a decrease in WASO, decreases in stages N1 and N2 sleep instability, and a decrease in the duration of EEG transient cortical arousals. The REM atonia index, a measure of REM sleep muscle tone, was not improved with clonazepam therapy of iRBD. However, the atonia index was increased during NREM sleep in the iRBD group compared to the other two groups, a new and interesting finding that merits further research. This study confirmed the previous study [9] that clonazepam modifies some aspects of NREM sleep (in a beneficial manner) in iRBD patients. Follow-up investigations should attempt to compare these results with findings from melatonin therapy of RBD.

The third study was a prospective, naturalistic follow-up of clonazepam treatment outcome in a series of 39 iRBD patients (mean age at diagnosis, 68 years; 74% male) [21]. Clonazepam had been offered as first-line treatment, with a mean initial

bedtime dose of 0.4 mg (range, 0.125–1.0 mg) and mean follow-up dose of 0.98 mg (range, 0.125–3.0 mg). The follow-up duration was a mean 29 months. Positive treatment response was reported to be 66.7%, using the stringent definition of "a complete elimination of sleep-related injuries and potentially injurious behaviors to self and/or bed partner." Furthermore, the frequency of disturbing dreams with violent and frightening content was also significantly reduced with clonazepam therapy. Another reassuring finding was that there was no increase in the Epworth Sleepiness Scale score after chronic clonazepam therapy of RBD compared to baseline. However, there was an increase in both level of tonic EMG activity and combined tonic/phasic EMG activity during REM sleep in the clonazepam-treated patients at follow-up compared to baseline, which confirmed a previous similar finding in iRBD patients [22]. Most likely this increased tonic/phasic EMG activity over time reflected an evolving synucleinopathy neurodegeneration in iRBD patients, which was not halted by clonazepam therapy. (A similar comparative study should be conducted for melatonin therapy of iRBD.) Finally, the authors of this study [21] modified their previously validated REM sleep behavior disorder questionnaire (RBDQ) to facilitate assessing treatment outcome in RBD, by creating a 3-month time frame for frequency of RBD events, with each item scored on a four-point scale (none; less than once per month; 1–2 times per month; ≥1 time weekly), with good internal consistency and with high correlation between the RBDQ-3M and the original RBDQ overall scale, dream-related subscale and behavioral subscale. Chapter 19 discusses the instruments used for RBD screening, the assessment of RBD severity, and monitoring treatment outcome.

25.3 Level C Pharmacotherapies of RBD

25.3.1 Dopaminergics

Levodopa, which has been used for over 50 years as the predominant therapy in Parkinson's disease (PD), has only limited efficacy in RBD. In a series of three patients with PD preceded by presumed RBD (no PSG was performed), levodopa was reportedly effective in controlling the presumed RBD [23]. However, during this earlier period, history-taking for RBD was not well established, and the lack of PSG documentation predisposed to potential large discrepancies between subjective complaints and objective findings, resulting in uncertainty in regard to the parasomnia diagnosis and the basis for improvement of motor symptoms in response to treatment. Conversely, a prospective case series in previously untreated PD patients reported the onset of RBD in less than 1 year after initiating levodopa therapy in 5/15 PD patients [24]. Clearly, levodopa therapy did not prevent the emergence of RBD in these PD patients. Of note, a systematic study of 35 PD patients found that those with RBD generally used higher doses of levodopa than those without RBD in the context of comparable disease stages [25]. This finding is consistent with other studies in PD indicating that comorbid RBD predicts a more aggressive course of disease.

Pramipexole, a dopamine receptor agonist, has been shown in four case series to be effective in 62–89% of patients with iRBD, RBD associated with mild cognitive impairment, or RBD with mild PD [26–29]. On the other hand, a prospective study of patients with combined RBD-PD found no benefit in reducing the severity or frequency of RBD when pramipexole was added to a stable levodopa regimen [30]. The starting dose of pramipexole in the therapy of RBD should be 0.125 mg at bedtime, with gradual increments by 0.125 mg, up to a maximum of 2–4 mg at bedtime.

Pramipexole appears to be most effective in RBD cases associated with frequent PLMs (in both NREM and REM sleep). PLMs in NREM sleep are a common PSG finding in RBD and are often responsive to dopaminergics. One investigation noted that compared to clonazepam-responsive RBD patients, pramipexole-responsive RBD patients had more mild disease at baseline as measured by the level of REM sleep atonia [28]. Similar to treating OSA in RBD (see Chap. 23), pramipexole may decrease nocturnal symptoms by reversing a sleep-fragmenting condition, viz., PLMs. Another pramipexole study in RBD patients reported a decrease in distressing nocturnal behaviors along with a decrease in PLMs, but no effect on REM sleep atonia [29]. Pramipexole therapy of RBD has recently been critically reviewed [31].

Rotigotine, a dopamine agonist of the non-ergoline class, has recently been shown to be partly effective in treating RBD symptoms in the setting of PD [32]. In a prospective open-label study, 11 PD patients with untreated RBD received rotigotine transdermal patches for up to 7 months as therapy of their PD. Severity of RBD symptoms before and after rotigotine therapy was evaluated by patient and bed partner interviews, a validated scale (RBDQ-HK, described above and in Chap. 19), and blinded assessments based on vPSG measures. Rotigotine improved PD and subjective sleep quality in the PD-RBD patients. Subjectively, RBD symptoms were improved, particularly the frequency and severity of abnormal RBD behaviors. However, objectively, the vPSG analyses found no differences in RBD-related sleep measures (a common theme with the pharmacotherapy of RBD).

25.3.2 Other Agents

These initial findings encourage the further study of dopaminergics in RBD, and suggest that these agents could be considered as RBD treatment options, especially in the setting of elevated PLMs among RBD patients with PD. The mixed therapeutic results with dopaminergic therapy of RBD may seem perplexing, given the strong link between RBD and PD/other synucleinopathies, and the eventual >80% phenoconversion from iRBD to a parkinsonism disorder (as described in Chaps. 4–6). Why shouldn't dopaminergic therapy be the first-line therapy of RBD? The negative answer to this logical question illustrates the complex neurochemistry, neuroanatomy, and neurophysiology subserving REM atonia and the phasic REM sleep motor-behavioral system. This is addressed in the basic science section (Chaps. 39, 42, 43). There is also a novel animal model of RBD (with clinical

implications) produced by genetic inactivation of glutamate neurons in the rat sublaterodorsal tegmental nucleus [33, 34].

Acetylcholinesterase inhibitors (AIs), which can trigger RBD in Alzheimer's disease [35, 36], have been reported as effective therapy of iRBD. Donepezil, in doses of 10–20 mg, was beneficial in two reports involving one case series of ten iRBD patients, with vPSG performed in 9/10 patients (although a 29-year-old man by description most likely had a NREM parasomnia along with RWA) [37, 38]; rivastigmine, in doses up to 6 mg at bedtime, was also reported to be effective in this series. Rivastigmine efficacy has also been reported in treatment-resistant, PSG-confirmed, RBD with PD, and in treatment-resistant, PSG-confirmed, RBD with mild cognitive impairment (MCI) [39, 40]. In these cases, the enhancement of central cholinergic neurotransmission with AI therapy was proposed to be the mechanism for the control of RBD not associated with dementia. However, donepezil therapy was not effective in controlling RBD severity or frequency in patients with neurodegenerative disorders [18]. Thus, AI therapy of RBD should be considered third-line therapy or else may be used as first-line therapy in symptomatic RBD associated with MCI, PD dementia, or dementia with Lewy bodies.

Sodium oxybate, an effective anti-cataplectic agent, has been reported to be effective monotherapy or supplemental therapy of RBD in six carefully described cases ($n = 5$, prior treatment-resistant cases; $n = 1$, *de novo* treated case) that will now be presented to allow a "first-hand feel" for the eventual successful management of treatment-resistant RBD cases. The first case was reported by Shneerson in 2009, involving a 66-year-old married man with a 2.5 year history of injurious dream-enacting behaviors documented to be caused by RBD with video-PSG (vPSG), in which he made running movements, aggressive arm gestures, shouting, and leaping from bed during REM sleep [41]. There was no neurological disorder, and so he was diagnosed with iRBD. After failing treatment with clonazepam, temazepam, zopiclone, melatonin, gabapentin, and clonidine, treatment with *sodium oxybate* was started, with control of RBD behaviors and nightmares within 4–5 days. This benefit was maintained, without further injury, at 1-year follow-up, at a dose of 4.5 gm at bedtime, without any side effects. The second case involved a man whose RBD persisted with nightly nightmares, screaming, and occasional injuries despite taking clonazepam 4 mg/night, melatonin 12 mg/night, and quetiapine 100 mg/night. However, with the addition of sodium oxybate at 3 g twice nightly, his RBD was almost completely controlled [19]. Sodium oxybate monotherapy was eventually achieved, with full ongoing control of the RBD. However, if he failed to take the sodium oxybate, RBD would invariably recur.

A third case involved a man in his late 60s with a 15-year history of PD and 20-year history of violent RBD episodes occurring 3–4 nights weekly, with recurrent injuries to himself and his wife [42]. Deep brain stimulation therapy of PD improved daytime motor PD symptoms, but the RBD worsened, with nightly aggressive episodes. After vPSG confirmation of RBD (and mild OSA; AHI = 8.5), sequential therapy with clonazepam (1 mg), melatonin (12 mg), prazosin, ramelteon, cyproheptadine, and eszopiclone was ineffective, and violent RBD episodes increased in frequency and severity. Sodium oxybate therapy was started, with the dose titrated to 2.5 g twice nightly. There was rapid and complete RBD symptom

resolution for 2 months, and then because of rare subsequent breakthrough episodes, the dose was increased to 3 g twice nightly, with complete control of RBD at 1.5 year follow-up. There were no reported side effects. Repeat vPSG on sodium oxybate therapy revealed the persistence of REM without atonia (RWA), without any dream-enacting behavior, and the AHI = 12.8.

Two other reported cases of iRBD treated with sodium oxybate involved 68- and 51-year-old males [43]. In the first case, there was a 10-year history of RBD, with multiple nightly dream-enacting episodes with beating and choking the bed partner, and sustaining injuries (e.g., fracturing his arm). vPSG confirmed RBD, but bedtime therapy with clonazepam (2 mg), alone or combined with carbamazepine (400 mg) and lamotrigine (25 mg), was inadequate and/or poorly tolerated. There was a temporary response to pramipexole (up to 0.45 mg) and melatonin (5 mg). Medical history was negative. Neurologic exam revealed fatigue and mild hyposmia. Sodium oxybate was started, with the dose titrated to 4.5 g twice nightly, with pramipexole 0.45 mg and melatonin 5 mg continued. The patient eventually reduced the dose to 4.5 g at bedtime. There was dramatic improvement of RBD noted by the patient and bed partner within the first weeks of therapy. Repeat vPSG revealed the persistence of RWA. Melatonin was withdrawn without worsening of RBD. However, pramipexole withdrawal resulted in clinical worsening of nocturnal behaviors, and so it was restarted. Actigraphy showed sustained resolution at 4-year follow-up. Benefit of combined sodium oxybate (4.5 g at bedtime) and pramipexole (0.45 mg at bedtime) was continued at 5.5-year follow-up, as confirmed by the patient and his wife. The only side effect reported was mild constipation.

In the second case, there was an 8-year history of RBD, with episodes occurring up to twice weekly with multiple injuries, including a fracture of one of his nasal bones, hitting and choking his wife during dream enactment of chasing thieves, and fighting. vPSG confirmed RBD, without sleep-disordered breathing. There was a temporary response to clonazepam, 2 mg alone, then together with melatonin 5 mg, and finally with pramipexole up to 0.36 mg, but in each case, he soon became refractory. Sodium oxybate, 1.5 g twice nightly, was added to clonazepam 2 mg at bedtime. There was dramatic improvement noted within first month with a decrease in frequency and intensity of the episodes. The bed partner confirmed the cessation of complex and violent episodes. Sporadic minor movements and sleep talking persisted. Repeat vPSG showed the persistence of RWA. An attempt at clonazepam withdrawal resulted in RBD relapse, and so he was maintained on 2 mg clonazepam at bedtime together with sodium oxybate 1.5 g twice nightly, with benefit maintained at 2.5-year follow-up. Mild morning sleep inertia was the only reported side effect. Neurologic exam did not detect any parkinsonism. The sixth reported case of sodium oxybate efficacy (as initial therapy) in RBD with violent, injurious dream-enacting behaviors, involved a 56-year-old male patient with comorbid narcolepsy type 1 [44]. Future systematic research on sodium oxybate therapy of RBD should include cohorts of patients with narcolepsy-cataplexy-RBD, and not just treatment-resistant iRBD or other types of symptomatic RBD. The mechanism(s) of action of sodium oxybate in the control of treatment-resistant cases of iRBD and PD-RBD, and in narcolepsy type 1-RBD remains to be elucidated.

Further support for the use of SO as effective therapy of RBD was found in a recent study on the effect of chin muscle tone during sleep with SO therapy of narcolepsy type 1 [45]. The analyses included short (<0.5 s) and long (>0.5 s) chin muscle activity indices per hour. A validated semiautomatic analysis of muscle tone was utilized. A total of 116 patients were studied, with PSG performed at baseline, 4 weeks after titration of SO to 4.5, 6, 9 g, or placebo, and after another 4 weeks on a stable SO dose. A major finding was that long (>0.5 s) chin muscle activity decreased significantly during REM sleep, especially with high doses of SO, thus encouraging its therapeutic use in RBD, particularly in RBD comorbid with narcolepsy type 1, and also in RBD treatment-resistant cases.

However, side effects from SO should be anticipated in some cases, including sexsomnia [46] and sleep-related eating disorder (SRED) [46], as reported in a case of a 41-year-old woman with narcolepsy type 1, whose therapy with SO induced the onset and recurrence of these two parasomnias, in which she would sexually assault her husband (at times culminating in full intercourse) while talking obscenely, and she would also go to the kitchen to eat "voraciously" (including immediately after having sex), for which she always had subsequent amnesia [47]. These parasomnias promptly resolved upon discontinuation of SO. (Sexsomnia and SRED are discussed in Chap. 27 on Parasomnia Overlap Disorder.)

Other therapies of iRBD or symptomatic RBD (apart from melatonin and melatonin receptor agonists that are discussed in Chap. 24) described in case reports and small case series reported to be effective include clonidine (a potent suppressor of REM sleep) [48], desipramine/imipramine [6, 49] (i.e. TCAs that can also trigger or aggravate RBD), paroxetine [50, 51], monoamine oxidase inhibitors [52], carbamazepine [53], zopiclone [54], temazepam [54], gabapentin [55], and cannabidiol [56]. The finding that paroxetine, an SSRI that can trigger or aggravate RWA/RBD in Caucasians [57]—along with fluoxetine [58], sertraline [59], and other SSRIs—was effective in controlling RBD in Japanese patients [50, 51] raises questions about ethnically mediated, divergent pharmacologic responses in RBD.

Yi-Gan San, an herbal preparation whose prescription is approved in Japan for treating insomnia, contains seven herbal ingredients, including Angelicae radix that has been reported to affect 5-HT2 and GABA receptors. Three cases of PSG-confirmed RBD from Japan have been reported in which the RBD (in a 60-year-old man and 74- and 87-year-old women) with aggressive dream enactment responded to Yi-Gan San therapy, taken at a dose of 2.5 gm ($n = 1$) or 7.5 gm ($n = 2$), with one patient also taking low-dose clonazepam (0.25 mg) [60].

25.4 Non-pharmacologic Therapies of RBD

Bed Alarm [61]. Exiting the bed while acting out a dream is a particularly high-risk behavior and may result in severe traumatic injury. Intriguingly, the low arousal threshold and rapid transition to alert wakefulness from REM sleep offers a therapeutic window to halt exiting the bed prior to sleep-related injury with RBD. Despite

apparent unconsciousness during REM sleep, the brain is readily responsive to complex auditory sound processing. This contrasts with the high arousal threshold of NREM sleep often demonstrated by the inability to redirect or wake up sleepwalkers (a NREM parasomnia). A study of patients with medication refractory RBD and sleep-related injury demonstrated the utility of a customized bed alarm that delivered a calming message at the onset of dream enactment behavior [61]. Ideal voices, typically those of family members, were identified, and commands to halt dream enactment behavior were then recorded (e.g., "Dave, you are having a dream, lay back down"). Subsequently, when the patient arose during sleep, the voice emanated from a bedside speaker on a repeating loop until the patient returned to lying down on the pressure pad.

Immunosuppressive therapy of RBD in cases associated with CNS autoimmune diseases and paraneoplastic disorders will be discussed by Iranzo in Chap. 8.

Pallidotomy was effective in one case of RBD associated with Parkinson's disease (PD) [62]. Whereas chronic bilateral subthalamic deep brain stimulation (DBS) was not effective for RBD in two reports [63, 64], in a recent report of three PD patients with RBD associated with parasomnia overlap disorder (POD: RBD + NREM sleep parasomnia, covered in Chap. 27), with these patients undergoing bilateral subthalamic DBS, one of the patients, a 70-year-old woman, demonstrated an impressive therapeutic response [65]. Episodes of dream enactment and confusional arousals were suppressed, sleep talking became rare, and sleep architecture markedly improved after DBS treatment. Also, comparing the PSG findings before vs. after DBS treatment, there was a 44% reduction in REM sleep chin tonic muscle activity and 8% reduction in REM sleep phasic muscle activity. In contrast, the other two RBD/POD patients in this DBS treatment group (males, 55 and 75 years old) had deterioration of their RBD/POD posttreatment. Interestingly, an isolated episode of RBD has been reported immediately following left subthalamic electrode implantation for the treatment of Parkinson's disease [66].

Finally, successful control of RBD with appropriate pharmacotherapy, or other somatic therapy, also usually controls the "environmental sleep disorder" [46] for the bed partner (i.e., wife) that had involved long-standing, recurrent sleep disruption and injuries from the RBD. This demonstrates how effective therapy of one person's sleep disorder, viz., RBD, can restore normal, uneventful, and restful sleep in the bed partner.

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