

BÖLÜM 15

ÇOCUK VE ERGENLERDE REM UYKUSU DAVRANIŞ BOZUKLUĞU

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Giriş

REM uykusu davranış bozukluğu (RUDB), ilk olarak 1986 yılında, Schenck ve ark. tarafından *yaşlı erkeklerde REM uykusuyla ilişkili bir parasomni* olarak tanımlanmıştır (1). İlk zamanlar, sadece yaşlı erkeklerde ortaya çıktığı düşünülürken, günümüzde çocuklar ve ergenlerde de görüldüğü bildirilmiştir. RUDB'nin temel özelliği, rüyaların harekete geçmesine neden olan REM atoni kaybıdır. Rüyanın içeriğine bağlı olarak, kişi kendine veya etrafındakilere zarar verebilir. Yetişkinlerde, RUDB'nin bir prodrom olabileceği söylenmiş; özellikle nörodejeneratif bozukluklar olmak üzere, narkolepsi, epilepsi ve antidepresan ilaçlarla ilişkisi gösterilmiştir (2).

Bu bozukluğun patofizyolojik mekanizmaları, Boeve ve ark. tarafından araştırılmıştır. RUDB'de, inhibitör beyin sapı motor mekanizmalarında düzensizlik vardır. İnsanlarda kesin yol belirlenmemiş olsa da, yapısal lezyonlarla ilişkili birkaç yayımlanmış insan RUDB vakasından elde edilen nörogörüntüleme verileri, bu bozukluğu dorsal orta beyin ve pons ile ilişkilendirmiştir. Ayrıca kedilerde yapılan çalışmalar, subcoeruleus bölgesinin önemli olduğunu gösterirken, sıçanlarda yapılanlar, RUDB'nin gelişimi için sublaterodorsal çekirdeği işaret etmektedir (3, 4).

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Melatonin, bu dozlarda iyi tolere edilme eğilimindedir, ara sıra hastalarda gastrointestinal sıkıntı veya baş ağrısı gelişir. Bildirilen diğer yan etkiler genellikle hafiftir ve uyku hâli, yorgunluk, baş dönmesi ve bilişsel değişikliği içerir (58).

RUDB'li 45 hastayı içeren retrospektif bir çalışmada, melatonin ve klonazepam benzer şekilde etkili görülmüş ve melatonin daha iyi tolere edilmiştir. Melatonin ile tedavi edilen hastaların yaklaşık üçte ikisi, semptomlarda en azından hafif iyileşme bildirmiştir ve %12'sinde RUDB davranışları tamamen düzelmiştir. Melatonin kullanan hastalar, klonazepam ile karşılaştırıldığında tedavi sonrası daha az düşme ve yaralanma bildirilmiştir (56).

Melatonin ve klonazepam tedavisinin başarısız olduğu hastalarda kolinerjik ajanlar yararlı olabilmektedir. Yapılan bir çalışmada, asetilkolinesteraz inhibitörü rivastigmin, Parkinson hastalığı (PH) ve RUDB hastalarında rüyayı gerçekleştirme davranışı epizodlarının sayısını azaltmıştır (60).

REM dışı uyku sırasında sık periyodik uzuv hareket bozukluğu (PUHB) olduğunda, pramipeksolün RUDB'yi etkili bir şekilde tedavi ettiği bildirilmiştir. Bu vakalarda, pramipeksolün gece motor aktivitesini pasifleştirmeye yardımcı olduğu ve altta yatan uykuda parçalanma durumu olan PUH bozukluğunda etkili görünmesi mümkündür (61-63).

Başarısı bildirilen diğer ajanlar arasında imipramin, karbamazepin, sodyum oksibat, triazolam, zopiklon, ketiapin ve klozapin bulunur (64-67).

Sonuç

Çocuk ve ergenlerde REM uykusu davranış bozukluğu (RUBD)'nin nadir olması, bu durumu tanımlamayı, teşhis etmeyi ve tedavi etmeyi zorlaştırır. Bununla birlikte, son yıllarda birkaç vaka raporunun mevcudiyeti, çocuk ve ergenlerde RUBD'nin varlığını doğrulamaktadır. Çocuk ve ergenlerde bu durumun etiyojilerini anlamak için yetişkinlerdeki bulgulara kıyasla daha fazla bilgiye ihtiyaç vardır.

Kaynaklar

1. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. *Sleep*. 1986;9(2):293-308.
2. Stores G. Rapid eye movement sleep behaviour disorder in children and adolescents. *Developmental Medicine & Child Neurology*. 2008;50(10):728-32.
3. Boeve BF. REM sleep behavior disorder: updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. *Annals of the New York Academy of Sciences*. 2010;1184(1):15-54.
4. Boeve B, Silber M, Saper C, Ferman T, Dickson D, Parisi J, et al. Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. *Brain*. 2007;130(11):2770-88.



5. Kang S-H, Yoon I-Y, Lee SD, Han JW, Kim TH, Kim KW. REM sleep behavior disorder in the Korean elderly population: prevalence and clinical characteristics. *Sleep*. 2013;36(8):1147-52.
6. Sateia MJ. International classification of sleep disorders. *Chest*. 2014;146(5):1387-94.
7. Haba-Rubio J, Frauscher B, Marques-Vidal P, Toriel J, Tობback N, Andries D, et al. Prevalence and determinants of rapid eye movement sleep behavior disorder in the general population. *Sleep*. 2018;41(2):zsx197.
8. Sasai-Sakuma T, Takeuchi N, Asai Y, Inoue Y, Inoue Y. Prevalence and clinical characteristics of REM sleep behavior disorder in Japanese elderly people. *Sleep*. 2020;43(8):zsaa024.
9. Lloyd R, Tippmann-Peikert M, Slocumb N, Kotagal S. Characteristics of REM sleep behavior disorder in childhood. *Journal of clinical sleep medicine*. 2012;8(2):127-31.
10. Nevsimalova S, Prihodova I, Kemlink D, Lin L, Mignot E. REM behavior disorder (RBD) can be one of the first symptoms of childhood narcolepsy. *Sleep medicine*. 2007;8(7-8):784-6.
11. Shukla G, Gupta A, Chakravarty K, Joseph AA, Ravindranath A, Mehta M, et al. Rapid eye movement (REM) sleep behavior disorder and REM sleep with atonia in the young. *Canadian Journal of Neurological Sciences*. 2020;47(1):100-8.
12. Nielsen T, Svob C, Kuiken D. Dream-enacting behaviors in a normal population. *Sleep*. 2009;32(12):1629-36.
13. Sheldon SH, Jacobsen J. REM-sleep motor disorder in children. *Journal of child neurology*. 1998;13(6):257-60.
14. Bjørnara KA, Dietrichs E, Toft M. REM sleep behavior disorder in Parkinson's disease—is there a gender difference? *Parkinsonism & related disorders*. 2013;19(1):120-2.
15. Teman PT, Tippmann-Peikert M, Silber MH, Slocumb NL, Auger RR. Idiopathic rapid-eye-movement sleep disorder: associations with antidepressants, psychiatric diagnoses, and other factors, in relation to age of onset. *Sleep medicine*. 2009;10(1):60-5.
16. Ferman T, Boeve B, Smith G, Lin S-C, Silber M, Pedraza O, et al. Inclusion of RBD improves the diagnostic classification of dementia with Lewy bodies. *Neurology*. 2011;77(9):875-82.
17. Schenck CH, Mahowald MW. Motor dyscontrol in narcolepsy: rapid-eye-movement (REM) sleep without atonia and REM sleep behavior disorder. *Annals of neurology*. 1992;32(1):3-10.
18. Rye DB, Johnston LH, Watts RL, Bliwise DL. Juvenile Parkinson's disease with REM sleep behavior disorder, sleepiness, and daytime REM onset. *Neurology*. 1999;53(8):1868-.
19. Coco DL, Cupidi C, Mattaliano A, Baiamonte V, Realmuto S, Cannizzaro E. REM sleep behavior disorder in a patient with frontotemporal dementia. *Neurological Sciences*. 2012;33(2):371-3.
20. Chokroverty S, Bhat S, Rosen D, Farheen A. REM behavior disorder in myotonic dystrophy type 2. *Neurology*. 2012;78(24):2004-.
21. Ebben MR, Shahbazi M, Lange DJ, Krieger AC. REM behavior disorder associated with familial amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis*. 2012;13(5):473-4.
22. Nomura T, Inoue Y, Takigawa H, Nakashima K. Comparison of REM sleep behaviour disorder variables between patients with progressive supranuclear palsy and those with Parkinson's disease. *Parkinsonism & related disorders*. 2012;18(4):394-6.
23. Boeve BF, Molano JR, Ferman TJ, Lin S-C, Bieniek K, Tippmann-Peikert M, et al. Validation of the Mayo Sleep Questionnaire to screen for REM sleep behavior disorder in a community-based sample. *Journal of Clinical Sleep Medicine*. 2013;9(5):475-80.
24. Thirumalai SS, Shubin RA, Robinson R. Rapid eye movement sleep behavior disorder in children with autism. *Journal of child neurology*. 2002;17(3):173-8.
25. Turner R, Allen W. REM sleep behavior disorder associated with narcolepsy in an adolescent: a case report. *Sleep Res*. 1990;19:302.
26. Vale TC, Fernandes do Prado LB, Fernandes do Prado G, Barsottini OGP, Pedrosa JL. Rapid eye movement sleep behavior disorder in paraneoplastic cerebellar degeneration: improvement with immunotherapy. *Sleep*. 2016;39(1):117-20.



27. Sabater L, Gaig C, Gelpi E, Bataller L, Lewerenz J, Torres-Vega E, et al. A novel non-rapid-eye movement and rapid-eye-movement parasomnia with sleep breathing disorder associated with antibodies to IgLON5: a case series, characterisation of the antigen, and post-mortem study. *The Lancet Neurology*. 2014;13(6):575-86.
28. Tribl GG, Trindade MC, Bittencourt T, Lorenzi-Filho G, Alves RC, de Andrade DC, et al. Wilson's disease with and without rapid eye movement sleep behavior disorder compared to healthy matched controls. *Sleep medicine*. 2016;17:179-85.
29. Elliott JE, Opel RA, Pleshakov D, Rachakonda T, Chau AQ, Weymann KB, et al. Posttraumatic stress disorder increases the odds of REM sleep behavior disorder and other parasomnias in Veterans with and without comorbid traumatic brain injury. *Sleep*. 2020;43(3):zsz237.
30. Boeve B, Dickson D, Olson E, Shepard J, Silber M, Ferman T, et al. Insights into REM sleep behavior disorder pathophysiology in brainstem-predominant Lewy body disease. *Sleep medicine*. 2007;8(1):60-4.
31. Manni R, Ratti P-L, Terzaghi M. Secondary "incidental" REM sleep behavior disorder: Do we ever think of it? *Sleep Medicine*. 2011;12:S50-S3.
32. Jianhua C, Xiuqin L, Quancai C, Heyang S, Yan H. Rapid eye movement sleep behavior disorder in a patient with brainstem lymphoma. *Internal medicine*. 2013;52(5):617-21.
33. McCarter SJ, Tippmann-Peikert M, Sandness DJ, Flanagan EP, Kantarci K, Boeve BF, et al. Neuroimaging-evident lesional pathology associated with REM sleep behavior disorder. *Sleep medicine*. 2015;16(12):1502-10.
34. Arnulf I. REM sleep behavior disorder: motor manifestations and pathophysiology. *Movement Disorders*. 2012;27(6):677-89.
35. Tabata H, Kuriyama A, Yamao F, Kitaguchi H, Shindo K. Suvorexant-induced dream enactment behavior in parkinson disease: a case report. *Journal of Clinical Sleep Medicine*. 2017;13(5):759-60.
36. Yeh S-B, Yeh P-Y, Schenck CH. Rivastigmine-induced REM sleep behavior disorder (RBD) in a 88-year-old man with Alzheimer's disease. *Journal of Clinical Sleep Medicine*. 2010;6(2):192-5.
37. Iranzo A, Santamaria J. Bisoprolol-induced rapid eye movement sleep behavior disorder. *The American journal of medicine*. 1999;107(4):390-2.
38. Rosenberg RS, Van Hout S. The American Academy of Sleep Medicine inter-scorer reliability program: respiratory events. *Journal of clinical sleep medicine*. 2014;10(4):447-54.
39. Fernández-Arcos A, Iranzo A, Serradell M, Gaig C, Santamaria J. The clinical phenotype of idiopathic rapid eye movement sleep behavior disorder at presentation: a study in 203 consecutive patients. *Sleep*. 2016;39(1):121-32.
40. D'Agostino A, Manni R, Limosani I, Terzaghi M, Cavallotti S, Scarone S. Challenging the myth of REM sleep behavior disorder: no evidence of heightened aggressiveness in dreams. *Sleep medicine*. 2012;13(6):714-9.
41. Sasai T, Inoue Y, Matsuura M. Do patients with rapid eye movement sleep behavior disorder have a disease-specific personality? *Parkinsonism & related disorders*. 2012;18(5):616-8.
42. Berry RB, Brooks R, Gamaldo CE, Harding SM, Marcus C, Vaughn BV. The AASM manual for the scoring of sleep and associated events. Rules, Terminology and Technical Specifications, Darien, Illinois, American Academy of Sleep Medicine. 2012;176:2012.
43. Neikrug AB, Ancoli-Israel S. Diagnostic tools for REM sleep behavior disorder. *Sleep medicine reviews*. 2012;16(5):415-29.
44. Eiser A, Schenck CH. Dreaming: A psychiatric view and insights from the study of parasomnias. *Schweizer Archiv für Neurologie und Psychiatrie*. 2005.
45. Howell MJ. Parasomnias: an updated review. *Neurotherapeutics*. 2012;9(4):753-75.
46. Li Y, Kang W, Yang Q, Zhang L, Zhang L, Dong F, et al. Predictive markers for early conversion of iRBD to neurodegenerative synucleinopathy diseases. *Neurology*. 2017;88(16):1493-500.



47. Soca R, Keenan JC, Schenck CH. Parasomnia overlap disorder with sexual behaviors during sleep in a patient with obstructive sleep apnea. *Journal of Clinical Sleep Medicine*. 2016;12(8):1189-91.
48. Cipolli C, Bonanni E, Maestri M, Mazzetti M, Murri L. Dream experience during REM and NREM sleep of patients with complex partial seizures. *Brain research bulletin*. 2004;63(5):407-13.
49. Yeh S-B, Schenck CH. Sleep-related screaming as a manifestation of frontal lobe epilepsy in a 8 year-old girl: case report with diagnostic polysomnographic and neuroradiological findings. *Acta Neurol Taiwan*. 2009;18:281-6.
50. Al-Biltagi MA. Childhood epilepsy and sleep. *World journal of clinical pediatrics*. 2014;3(3):45.
51. Mysliwiec V, Brock MS, Creamer JL, O'Reilly BM, Germain A, Roth BJ. Trauma associated sleep disorder: a parasomnia induced by trauma. *Sleep medicine reviews*. 2018;37:94-104.
52. Schenck CH, Lee SA, Bornemann MAC, Mahowald MW. Potentially lethal behaviors associated with rapid eye movement sleep behavior disorder: review of the literature and forensic implications. *Journal of forensic sciences*. 2009;54(6):1475-84.
53. Howell MJ, Arneson PA, Schenck CH. A novel therapy for REM sleep behavior disorder (RBD). *Journal of Clinical Sleep Medicine*. 2011;7(6):639-44A.
54. Schenck CH, Mahowald MW. Rapid eye movement sleep parasomnias. *Neurologic clinics*. 2005;23(4):1107-26.
55. Ferri R, Zucconi M, Marelli S, Plazzi G, Schenck CH, Ferini-Strambi L. Effects of long-term use of clonazepam on nonrapid eye movement sleep patterns in rapid eye movement sleep behavior disorder. *Sleep medicine*. 2013;14(5):399-406.
56. McCarter SJ, Boswell CL, Louis EKS, Dueffert LG, Slocumb N, Boeve BF, et al. Treatment outcomes in REM sleep behavior disorder. *Sleep medicine*. 2013;14(3):237-42.
57. Chouinard G. Issues in the clinical use of benzodiazepines: potency, withdrawal, and rebound. *Journal of Clinical Psychiatry*. 2004;65:7-12.
58. McGrane IR, Leung JG, Louis EKS, Boeve BF. Melatonin therapy for REM sleep behavior disorder: a critical review of evidence. *Sleep medicine*. 2015;16(1):19-26.
59. Kunz D, Mahlberg R. A two-part, double-blind, placebo-controlled trial of exogenous melatonin in REM sleep behaviour disorder. *Journal of sleep research*. 2010;19(4):591-6.
60. Di Giacopo R, Fasano A, Quaranta D, Marca GD, Bove F, Bentivoglio AR. Rivastigmine as alternative treatment for refractory REM behavior disorder in Parkinson's disease. *Movement disorders*. 2012;27(4):559-61.
61. Sasai T, Matsuura M, Inoue Y. Factors associated with the effect of pramipexole on symptoms of idiopathic REM sleep behavior disorder. *Parkinsonism & related disorders*. 2013;19(2):153-7.
62. Sasai T, Inoue Y, Matsuura M. Effectiveness of pramipexole, a dopamine agonist, on rapid eye movement sleep behavior disorder. *The Tohoku journal of experimental medicine*. 2012;226(3):177-81.
63. Rutten S, van der Ven PM, Weintraub D, Pontone GM, Leentjens AF, Berendse HW, et al. Predictors of anxiety in early-stage Parkinson's disease—Results from the first two years of a prospective cohort study. *Parkinsonism & related disorders*. 2017;43:49-55.
64. Committee SoP, Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, et al. Best practice guide for the treatment of REM sleep behavior disorder (RBD). *Journal of Clinical Sleep Medicine*. 2010;6(1):85-95.
65. Anderson KN, Shneerson JM. Drug treatment of REM sleep behavior disorder: the use of drug therapies other than clonazepam. *Journal of Clinical Sleep Medicine*. 2009;5(3):235-9.
66. Gagnon J-F, Postuma RB, Montplaisir J. Update on the pharmacology of REM sleep behavior disorder. *Neurology*. 2006;67(5):742-7.
67. Liebenthal J, Valerio J, Ruoff C, Mahowald M. A case of rapid eye movement sleep behavior disorder in Parkinson disease treated with sodium oxybate. *JAMA neurology*. 2016;73(1):126-7.