

BÖLÜM 17

ÇOCUK VE ERGENLERDE MADDE VEYA İLAÇLARIN YOL AÇTIĞI UYKU BOZUKLUKLARI

Cansu Pınar YAVAŞ¹

Giriş

Uyku-uyanıklık düzenlemesinde yer alan nöronal mekanizmalar üzerine yapılan araştırmalar, uyku ve uyanıklık durumunun, hipotalamus ve beyin sapında bulunan uyanıklığı ve uykuyu düzenleyen çekirdekler arasındaki karmaşık bir etkileşim tarafından kontrol edildiğini göstermektedir (1, 2). Uyanıklığı sağlayan nöronlar, hipotalamusta oreksinerjik ve histaminerjik çekirdekleri, beyin sapında kolinerjik çekirdekleri, lokus seruleusta adrenerjik çekirdekleri, rafe çekirdeklerinde serotonerjik ve orta beyin ventral tegmental alanda dopaminerjik çekirdekleri içerir (3). Uyku, bazal ön beyin, ventrolateral preoptik alan ve ön hipotalamustaki çekirdekler tarafından inhibitör nörotransmitterler gama-aminobütirik asit (GABA) ve galanin aracılığıyla desteklenir (3). Uykunun homeostatik düzenlenmesinde rol oynadığı öne sürülen adenosin, bazal ön beyin ve beyin sapındaki antikolinerjik aktivite yoluyla uykuyu artırabilir. (3). Prostaglandin D2, nitrik oksit ve sitokinler dâhil olmak üzere somnojenler insanlarda, uykuyu [çoğunlukla NREM (non-rapid eye movement) uyku yu] artırır (4). REM (rapid eye movement) uyku indüksiyon bölgeleri ise ağırlıklı olarak glutamaterjik nöronları içerir (5). Bu nedenle, uyku-uyanıklık düzenlemesinde yer alan reseptörlerde farmakolojik etkileri olan ilaçların, uyku-uyanıklık davranışı üzerinde de etkileri olabilir (3). Bu etkiler, tedavi edici (uykuyu iyileştirme veya uyanıklığı artırma

¹ Uzm. Dr., Zonguldak Kadın Doğum ve Çocuk Hastalıkları Hastanesi, Çocuk Psikiyatri Kliniği, cpnrnsn@gmail.com



(sekiz ila on iki saat) göre kötüye kullanıma daha yatkındır (60).

Wu ve ark., ergenlerin önemli bir bölümünün esrar ve uçucu maddeler gibi diğer ilaçları denemeden önce opioidlerle deneyim kazandığını gözlemlemiştir (72). Yoğun beyin gelişimi sırasında opioidlere maruz kalmanın, gençler için bilinmeyen ve potansiyel olarak ciddi sonuçları olabilir (73). Opioidlerin uyku üzerindeki etkileri birçok araştırmacı tarafından incelenmiştir. Dimsdale ve ark., 42 sağlıklı yetişkinde, tek doz sürekli salımlı morfin ve metadon uygulamasının uyku üzerindeki etkisini araştırmıştır (74). Her iki opioidin oral yoldan verilmesinin, derin uyku yüzdesini azalttığı ve evre 2 uykuyu yüzdesini artırdığı bildirilmiştir (74). Araştırmacılar, evre 2 uykuda gözlenen artışın, kronik opioid kullanımına bağlı yorgunluğu artırabileceğini öne sürmüştür (74). Opioidlerden çekilme, uykusuzluğa ve REM uykusunda uzun süreli rebounda neden olur (75). Kronik opioid kullanımı, özellikle metadon, artan uykuda solunum bozukluğu ve merkezî uyku apnesi sıklığı ile ilişkilendirilmiştir (76). Reçeteli opioidlerin kullanımı, ergenlerde büyüyen bir sorundur. Yaygın kullanımları, kolay erişimleri ve yüksek bağımlılık potansiyelleri, istismar riskine karşı savunmasız olan gençlerin dikkatli olmasını ve sürekli eğitimini gerektirmektedir (30).

Sonuç

Ergenlerde uyku ve madde kullanım bozukluklarının yaygınlık oranı yüksektir. Tanınmayan ve tedavi edilmeyen uyku bozuklukları ve madde bağımlılığının sonuçları, yalnızca ergenlik döneminde değil, yaşamın ilerleyen dönemlerinde de önemli tıbbi, psikososyal ve ekonomik sorunlara yol açmaktadır. Bu bozukluklar, önemli oranda eksik teşhis edilmektedir; ayrıca, çift yönlü ilişkilerinin anlaşılması, en iyi tedavi seçeneklerini ve yöntemlerini engellemektedir. Bu nedenle, gençlerde uyku düzeni ve madde kullanımını araştırmak ve gençlere danışmanlık vermek çok önemlidir.

Kaynaklar

1. Szabadi E. Drugs for sleep disorders: mechanisms and therapeutic prospects. *Br J Clin Pharmacol.* 2006;61(6):761.
2. Saper CB, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. *Nature.* 2005;437(7063):1257-1263.
3. Schweitzer PK, Randazzo AC. Drugs that Disturb Sleep and Wakefulness. *Princ Pract Sleep Med.* 2017;480-498.
4. Monti JM. The neurotransmitters of sleep and wake, a physiological reviews series. *Sleep Med Rev.* 2013;17(4):313-315.
5. Luppi PH, Clément O, Fort P. Paradoxical (REM) sleep genesis by the brainstem is under hypothalamic control. *Curr Opin Neurobiol.* 2013;23(5):786-792.



6. Van Gastel A. Drug-Induced Insomnia and Excessive Sleepiness. *Sleep Med Clin.* 2018;13(2):147-159.
7. Nebes RD, Pollock BG, Houck PR, et al. Persistence of cognitive impairment in geriatric patients following antidepressant treatment: a randomized, double-blind clinical trial with nortriptyline and paroxetine. *J Psychiatr Res.* 2003;37(2):99-108.
8. Claghorn JL, Mathew RJ, Weinman ML, et al. Daytime sleepiness in depression. *J Clin Psychiatry.* 1981;42(9):342-343.
9. Benca RM, Obermeyer WH, Thisted RA, et al. Sleep and psychiatric disorders. A meta-analysis. *Arch Gen Psychiatry.* 1992;49(8):651-670.
10. Patel DR, Feucht C, Brown K, et al. Pharmacological treatment of anxiety disorders in children and adolescents: a review for practitioners. *Transl Pediatr.* 2018;7(1):23.
11. Chiu S, Leonard HL. Antidepressants I: selective serotonin reuptake inhibitors. *Pediatr Psychopharmacol Princ Pract.* 2002;274.
12. Armitage R, Emslie G, Rintelmann J. The effect of fluoxetine on sleep EEG in childhood depression: a preliminary report. *Neuropsychopharmacology.* 1997;17(4):241-245.
13. Schenck CH, Mahowald MW, Kim SW, et al. Prominent eye movements during NREM sleep and REM sleep behavior disorder associated with fluoxetine treatment of depression and obsessive-compulsive disorder. *Sleep.* 1992;15(3):226-235.
14. Sharpley AL, Williamson DJ, Attenburrow ME, et al. The effects of paroxetine and nefazodone on sleep: a placebo controlled trial. *Psychopharmacology (Berl).* 1996;126(1):50-54.
15. Doerr JP, Spiegelhalder K, Petzold F, et al. Impact of escitalopram on nocturnal sleep, day-time sleepiness and performance compared to amitriptyline: a randomized, double-blind, placebo-controlled study in healthy male subjects. *Pharmacopsychiatry.* 2010;43(5):166-173.
16. van Bommel AL, van den Hoofdakker RH, Beersma DG, et al. Changes in sleep polygraphic variables and clinical state in depressed patients during treatment with citalopram. *Psychopharmacology (Berl).* 1993;113(2):225-230.
17. Jindal RD, Friedman ES, Berman SR, et al. Effects of sertraline on sleep architecture in patients with depression. *J Clin Psychopharmacol.* 2003;23(6):540-548.
18. DeMartinis NA, Winokur A. Effects of psychiatric medications on sleep and sleep disorders. *CNS Neurol Disord Drug Targets.* 2007;6(1):17-29.
19. Oberndorfer S, Saletu-Zyhlarz G, Saletu B. Effects of selective serotonin reuptake inhibitors on objective and subjective sleep quality. *Neuropsychobiology.* 2000;42(2):69-81.
20. Winkelman JW, James L. Serotonergic antidepressants are associated with REM sleep without atonia. *Sleep.* 2004;27(2):317-321.
21. Rottach KG, Schaner BM, Kirch MH, et al. Restless legs syndrome as side effect of second generation antidepressants. *J Psychiatr Res.* 2008;43(1):70-75.
22. Roux FJ, Kryger MH. Medication effects on sleep. *Clin Chest Med.* 2010;31(2):397-405.
23. Holshoe JM. Antidepressants and sleep: a review. *Perspect Psychiatr Care.* 2009;45(3):191-197.
24. Wilson S, Argyropoulos S. Antidepressants and sleep: a qualitative review of the literature. *Drugs.* 2005;65(7):927-947.
25. Mayers AG, Baldwin DS. Antidepressants and their effect on sleep. *Hum Psychopharmacol.* 2005;20(8):533-559.
26. Ivanenko A. Sleep and psychiatric disorders in children and adolescents. *Sleep Psychiatr Disord Child Adolesc.* 2008.
27. Barnett SR, Riddle MA. Anxiolytics: benzodiazepines, buspirone, and others. *Pediatr Psychopharmacol Princ Pract.* 2002;341.
28. Shader RI, Greenblatt DJ. Use of benzodiazepines in anxiety disorders. *N Engl J Med.* 1993;328(19):1398-1405.
29. Popoviciu L, Corfariu O. Efficacy and safety of midazolam in the treatment of night terrors in children. *Br J Clin Pharmacol.* 1983;16 Suppl 1(Suppl 1):97S-102S.



30. Gromov I, Gromov D. Sleep and substance use and abuse in adolescents. *Child Adolesc Psychiatr Clin N Am.* 2009;18(4):929-946.
31. Krystal AD, Goforth HW, Roth T. Effects of antipsychotic medications on sleep in schizophrenia. *Int Clin Psychopharmacol.* 2008;23(3):150-160.
32. Stahl S. *Stahl's essential psychopharmacology : neuroscientific basis and practical application.* Cambridge ;;New York: Cambridge University Press; 2008. 608 p.
33. Findling RL, Steiner H, Weller EB. Use of antipsychotics in children and adolescents. *J Clin Psychiatry.* 2005;66 Suppl 7:29-40.
34. Sharpley AL, Attenburrow ME, Hafizi S, Cowen PJ. Olanzapine increases slow wave sleep and sleep continuity in SSRI-resistant depressed patients. *J Clin Psychiatry.* 2005;66(4):450-454.
35. Campbell M, Adams PB, Small AM, et al. Lithium in hospitalized aggressive children with conduct disorder: a double-blind and placebo-controlled study. *J Am Acad Child Adolesc Psychiatry.* 1995;34(4):445-53.
36. Klemfuss H. Rhythms and the pharmacology of lithium. *Pharmacol Ther.* 1992;56(1):53-78.
37. Obermeyer WH, Benca RM. Effects of drugs on sleep. *Neurol Clin.* 1996;14(4):827-840.
38. Friston KJ, Sharpley AL, Solomon RA, et al. Lithium increases slow wave sleep: possible mediation by brain 5-HT₂ receptors?. *Psychopharmacology (Berl).* 1989;98(1):139-140.
39. Declerck AC, Wauquier A. Influence of antiepileptic drugs on sleep patterns. *Epilepsy Res Suppl.* 1991;2:153-163.
40. Placidi F, Diomedi M, Scalise A, et al. Effect of anticonvulsants on nocturnal sleep in epilepsy. *Neurology.* 2000;54(5 Suppl 1):25-32.
41. Cohen-Zion M, Ancoli-Israel S. Sleep in children with attention-deficit hyperactivity disorder (ADHD): a review of naturalistic and stimulant intervention studies. *Sleep Med Rev.* 2004;8(5):379-402.
42. Green WH. *Child and adolescent clinical psychopharmacology.* Lippincott Williams & Wilkins; 2007.
43. Novak M, Shapiro CM. Drug-induced sleep disturbances. Focus on nonpsychotropic medications. *Drug Saf.* 1997;16(2):133-149.
44. Wang GS, Hoyte C. Common Substances of Abuse. *Pediatrics in review.* 2018; 39(8), 403-414.
45. Merz F. United Nations Office on Drugs and Crime: World Drug Report 2017. 2017. *SIRI-US-Zeitschrift für Strategische Analysen,* 2(1), 85-86.
46. Aly SM, Omran A, Gaulier J-M, et al. Substance abuse among children. *Arch Pediatr.* 2020 Nov;27(8):480-484.
47. Saarenpää-Heikkilä O, Laippala P, Koivikko M. Subjective daytime sleepiness and its predictors in Finnish adolescents in an interview study. *Acta Paediatr.* 2001;90(5):552-557.
48. D'Angiulli A, Grunau P, Maggi S, et al. Electroencephalographic correlates of prenatal exposure to alcohol in infants and children: a review of findings and implications for neurocognitive development. *Alcohol.* 2006;40(2):127-133.
49. Brower KJ. Alcohol's effects on sleep in alcoholics. *Alcohol Res Heal J Natl Inst Alcohol Abuse Alcohol.* 2001;25(2):110-125.
50. Brower KJ, Aldrich MS, Robinson EA, et al. Insomnia, self-medication, and relapse to alcoholism. *Am J Psychiatry.* 2001;158(3):399-404.
51. Patten CA, Choi WS, Gillin JC, et al. Depressive symptoms and cigarette smoking predict development and persistence of sleep problems in US adolescents. *Pediatrics.* 2000;106(2):E23.
52. Phillips BA, Danner FJ. Cigarette smoking and sleep disturbance. *Arch Intern Med.* 1995;155(7):734-737.
53. Shin C, Joo S, Kim J, et al. Prevalence and correlates of habitual snoring in high school students. *Chest.* 2003;124(5):1709-1715.
54. Morgan KJ, Stults VJ, Zabik ME. Amount and dietary sources of caffeine and saccharin intake by individuals ages 5 to 18 years. *Regul Toxicol Pharmacol.* 1982;2(4):296-307.



55. Ellison RC, Singer MR, Moore LL, et al. Current caffeine intake of young children: amount and sources. *J Am Diet Assoc.* 1995 Jul;95(7):802-804.
56. Strain EC, Mumford GK, Silverman K, et al. Caffeine dependence syndrome. Evidence from case histories and experimental evaluations. *JAMA.* 1994 Oct;272(13):1043-1048.
57. Crouch BI, Caravati EM, Booth J. Trends in child and teen nonprescription drug abuse reported to a regional poison control center. *Am J Heal Pharm AJHP Off J Am Soc Heal Pharm.* 2004; 61(12):1252-1257.
58. Karacan I, Thornby JI, Anch M, et al. Dose-related sleep disturbances induced by coffee and caffeine. *Clin Pharmacol Ther.* 1976;20(6):682-689.
59. Pollak CP, Bright D. Caffeine consumption and weekly sleep patterns in US seventh-, eighth-, and ninth-graders. *Pediatrics.* 2003;111(1):42-46.
60. Conroy DA, Arnedt JT, Brower KJ, et al. Sleep and substance use and abuse. In: Kramer M, Pandi-Perumal SR, editors. *Sleep and Mental Illness.* Cambridge: Cambridge University Press; 2010. p. 341-352.
61. Schierenbeck T, Riemann D, Berger M, et al. Effect of illicit recreational drugs upon sleep: cocaine, ecstasy and marijuana. *Sleep Med Rev.* 2008 Oct;12(5):381-389.
62. Murillo-Rodriguez E, Blanco-Centurion C, Sanchez C, et al. Anandamide enhances extracellular levels of adenosine and induces sleep: an in vivo microdialysis study. *Sleep.* 2003;26(8):943-947.
63. Nicholson AN, Turner C, Stone BM, et al. Effect of Delta-9-tetrahydrocannabinol and cannabidiol on nocturnal sleep and early-morning behavior in young adults. *J Clin Psychopharmacol.* 2004;24(3):305-313.
64. Dahl RE, Scher MS, Williamson DE, et al. A longitudinal study of prenatal marijuana use. Effects on sleep and arousal at age 3 years. *Arch Pediatr Adolesc Med.* 1995;149(2):145-150.
65. Bolla KI, Lesage SR, Gamaldo CE, et al. Sleep disturbance in heavy marijuana users. *Sleep.* 2008 Jun;31(6):901-908.
66. McGregor C, Srisurapanont M, Jittiwutikarn J, et al. The nature, time course and severity of methamphetamine withdrawal. *Addiction.* 2005 Sep;100(9):1320-1329.
67. Montoya AG, Sorrentino R, Lukas SE, et al. Long-term neuropsychiatric consequences of "ecstasy" (MDMA): a review. *Harv Rev Psychiatry.* 2002;10(4):212-220.
68. Baylen CA, Rosenberg H. A review of the acute subjective effects of MDMA/ecstasy. *Addiction.* 2006;101(7):933-947.
69. Cerdá M, Santaella J, Marshall BDL, et al. Nonmedical prescription opioid use in childhood and early adolescence predicts transitions to heroin use in young adulthood: a national study. *J Pediatr.* 2015;167(3):605-612.
70. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med.* 2016;374(2):154-163.
71. Carlson RG, Nahhas RW, Martins SS, et al. Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: A natural history study. *Drug Alcohol Depend.* 2016;160:127-134.
72. Wu L-T, Pilowsky DJ, Schlenger WE. High prevalence of substance use disorders among adolescents who use marijuana and inhalants. *Drug Alcohol Depend.* 2005;78(1):23-32.
73. Compton WM, Volkow ND. Major increases in opioid analgesic abuse in the United States: concerns and strategies. *Drug Alcohol Depend.* 2006;81(2):103-107.
74. Dimsdale JE, Norman D, DeJardin D, et al. The effect of opioids on sleep architecture. *J Clin sleep Med JCSM Off Publ Am Acad Sleep Med.* 2007;3(1):33-36.
75. Kay DC, Eisenstein RB, Jasinski DR. Morphine effects on human REM state, waking state and NREM sleep. *Psychopharmacologia.* 1969;14(5):404-416.
76. Wang D, Teichtahl H. Opioids, sleep architecture and sleep-disordered breathing. *Sleep Med Rev.* 2007;11(1):35-46.