35.d Ağrı Tedavisinde Motor Korteks ve Derin Beyin Stimülasyonu

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Giriş

Ağrı Uluslararası Ağrı Araştırmaları Teşkilatı (IASP) tarafından yapılan tanımlamaya göre; "Bedenin herhangi bölgesinde hissedilen, altta yatan organik bir neden olsun ya da olmasın, bireyin önceki tecrübeleri ile ilgili sensoryal, emosyonel, rahatsız edici bir duygu deneyimi olarak tanımlanır (1). Ağrı kişilerin hayatında büyük öneme sahip olan, günlük yaşamlarını kısıtlayan bir durumdur. Ağrının süresi uzayıp kronikleştikçe de etkisi daha da önem kazanmaktadır. Ağrıyı süresine göre akut ve kronik ağrı şeklinde 2 gruba ayırabiliriz. Akut ağrı, vücudun herhangi bir bölgesinde meydana gelen zedelenme sonrasında ortaya çıkan kişinin hoşuna gitmeyen duyusal deneyim olarak tanımlanmaktadır (2). Kronik ağrı; beklenenden daha uzun süren (3-6 ay) veya iyileşme sürecinden sonra devam eden ağrıdır. Doku hasarı ile neden olduğu lezyon arasında yer, zaman ve şiddet açısından net bir ilişki bulunmamaktadır. Doku hasarı kaybolduktan sonra da ağrı devam etmektedir (3,4).

Kişilerin ağrıya karşı duyarlılığının farklı olduğunu bilmekteyiz. Bu farklılığın nedenlerine baktığımızda reseptör duyarlılığı ve sayılarının yanı sıra kişinin yaşam şekli, eğitim seviyesi, cinsiyet, dil, din gibi çeşitli faktörlerin de etkili olduğunu görmekteyiz (6).

1-Ağrının Nöroanatomisi

Nosiseptör denilen özelleşmiş reseptörler tarafından algılanan ağrı reseptörde bir reseptör potansiyeli (jeneratör potansiyeli) oluşturur. Reseptör potansiyelinin yeterli büyüklüğe (eşik) ulaşması ile ilk aksiyon potansiyeli meydana gelir. Bunun sonucunda aktive olan nosiseptörlerin aracılığıyla keskin, iğneleyici ve iyi lokalize edilebilen bir ağrı oluşturur. Aδ lifleri ile hızlı – keskin ağrı (birincil ağrı / 30 m/sn), C lifleri ile de yavaş kronik ağrı (ikincil ağrı / 0,5-2 m/sn) taşınır (7,8). Nosiseptörlerin somaları spinal kordun dorsal kök ganglionunda yerleşmiş ağrı yolağının ilk nöronlarıdır. İkinci sıra nöronlar ise, spinal kordun dorsal boynuzunda bulunurlar. Bu nöronların akson uzantıları spinotalamik traktusu oluşturmaktadır. Spinotalamik traktusun lateral kolu ağrının uyaran lokalizasyonunu, yoğunluğu ve kalitesi ile ilişkili diskrimitif yönünü taşımada; medial kolu ise ağrılı deneyimin hoş olmayan yönü ile ilişkili affektif yönü olabileceği düşünülmektedir. Üçüncü sıra nöronlar talamusta yer alır. Ağrının affektif kısmı, orta beyin retiküler formasyonu bağlantısı üzerinden talamusun intralaminer çekirdeklerine gelir, diskriminatif kısım ise talamusun ventral posterior lateral (VPL) ve medial (VPM) çekirdeklerine ulaşabileceği söylenilmektedir (8). Özetle; anterolateral sistem dediğimiz medial lemniskus sistem lateral spinotalamik traktus yolu ile birincil ağrının taşınımında görevliyken medial spinotalamik traktus ise ikincil ağrı iletimini gerçekleşmektedir (7,8).

Ağrı bu iki yolak ile santral sinir sistemine ulaştıktan sonra kortekste birçok alan ile iç içe ilişkili geniş ağrı merkezlerini etkiler. Kortekste ağrı aktivasyonunun yanı sıra ağrının inhibisyonunda da etkili alanlar mevcuttur. Bu anti-nosiseptif

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KAYNAKLAR

1. Wıttınk, H., Mıchel,T. Chronic Pain Management for Physical Therapists. *USA: Elsevier Science*, 2002, page 4.
2. Güleç, G., Güleç, S. Ağrı ve Davranışı. *Ağrı*, 2006, 18(4): 5–9.
3. Çeliker, R. Kronik ağrı sendromları. *Türk Fiz Tıp Rehab Dergi*si, 2005, 51: 14–18.
4. Hall-Lord, M., Larsson, G., Steen, B. Chronic pain and distess in older people: A Cluster analysis. *International Journal of Nursing Practice*, 1999, 5: 78–85.
5. http://www.iasp-pain.org/PublicationsNews/Content.aspx?ItemNumber=1673
6. Tan E. Nöropatik Ağrı. Ankara, Türkiye, Nobel Matbaası, 2009; 1-63.
7. Velioğlu S.K. Ağrı Anatomisi: Ağrı Yolakları, Beyin Sapı ve Beyin. *Türk Klinikleri Dergisi Nöroloji*, 2017; 10(4): 329-335.
8. Savrun F. Ağrıda Nörofizyolojik Yöntemlerin Yeri. *Türk Klinikleri Dergisi Nöroloji*, 2017; 10(4): 339-347.
9. Ertekin C. Yegül İ (Editör). Ağrının nöroanatomisi ve nörofizyolojisi ağrı ve tedavisi. İzmir, Türkiye, Yapım Matbaacılık, 1993; 1-18.
10. Raj P.P. Erdine S. (Editör) *Ağrı taksonomisi*. İstanbul, Türkiye, Alemdar Ofset, 2000; 12-20.
11. Barrett K.E. (Ed. Gökbel H.). *Ganong'un Tıbbi Fizyolojisi*. İstanbul, Türkiye, Nobel Tıp Kitapevleri, 2015; 157-173.
12. Kurtcan S, Toprak H, Aralaşmak A. Ağrı Görüntülenmesi. *Türk Klinikleri Dergisi Nöroloji*, 2017; 10(4): 335-339.
13. Melzack R,Wall P.D. Pain Mechanism: a New Theory. Science 1965; 150(3699): 971-978.
14. Tsubokawa T, Katayama Y, Yamamoto T, Hirayama T, KoyamaS: Chronic motor cortex stimulation for the treatment ofcentral pain. *Acta Neurochir Suppl (Wien),* 1991, 52:137-139.
15. Krushelnytskyy MD, Carlstrom LP, Klassen BT, Lundstrom BN, Paek SB, Lavrov IA, Stead SM, Sandroni P, Lee KH: Chronic subdural cortical stimulation for phantom limb pain: Report of a series of two cases. *Acta Neurochir (Wien)*, 2019 (Epub ahead of print).
16. Levy R, Deer TR, Henderson J. Intracranial neurostimulation for pain control: a review. *Pain Phys.* 2010;**13**:157–165.
17. Nguyen JP, et al. Motor cortex stimulation in the treatment of central and neuropathic pain. *Arch. Med. Res.* 2000;**31**:263–265. doi: 10.1016/S0188-4409(00)00078-3.
18. Fontaine D, Hamani C, Lozano A. Efficacy and safety of motor cortex stimulation for chronic neuropathic pain: critical review of the literature - Clinical article. *J. Neurosurg.* 2009;**110**:251–256. doi: 10.3171/2008.6.17602.
19. Honey CM, Tronnier VM, Honey CR. Deep brain stimulation versus motor cortex stimulation for neuropathic pain: a minireview of the literature and proposal for future research. *Comput. Struct. Biotechnol. J.* 2016;**14**:234–237. doi: 10.1016/j.csbj.2016.06.003.
20. Brown JA: Motor cortex stimulation. *Neurosurg Focus,*2001, 11:E5.
21. Garcia-Larrea L, Peyron R, Mertens P, Gregoire MC, Lavenne F, Le Bars D, Convers P, Mauguiere F, Sindou M, Laurent B: Electrical stimulation of motor cortex for pain control: A combined PET-scan and electrophysiological study. *Pain*, 1999, 83:259-273.
22. Garcia-Larrea L, Peyron R, Mertens P, Laurent B, Mauguiere F, Sindou M: Functional imaging and neurophysiological assessment of spinal and brain therapeutic modulation in humans. *Arch Med Res*, 2000, 31:248-257.
23. Fonoff ET, Dale CS, Pagano RL, Paccola CC, Ballester G, Teixeira MJ, Giorgi R: Antinociception induced by epidural motor cortex stimulation in naive conscious rats is mediated by the opioid system. , *Behav Brain Res*, 2009, 196:63-70.
24. Maarrawi J, Peyron R, Mertens P, Costes N, Magnin M, Sindou M, Laurent B, Garcia-Larrea L: Motor cortex stimulation for pain control induces changes in the endogenous opioid system. *Neurology*, 2007, 69:827-834.
25. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. *Pain*, 1975, 1:277–299.
26. Melzack R, Terrence C, Fromm G, et al: Trigeminal neuralgia and atypical facial pain: use of the McGill Pain Questionnaire for discrimination and diagnosis. *Pain*, 1986, 27:297–302.
27. Mogilner AY, Rezai AR: Epidural motor cortex stimulation with functional imaging guidance. *Neurosurg Focus*, 2001, 11:E4.
28. Edwards CA, Kouzani A, Lee KH, Ross EK: Neurostimulation devices for the treatment of neurologic disorders. *Mayo Clin Proc*, 2017, 92:1427-1444.
29. Shils J, Arle J: Treatment applications of cortical stimulation. In: Winn HR (ed), Youmans Neurological Surgery. Philadelphia (PA): *Elsevier Saunders,* 2011:1059-1064.
30. Hussein AE, Esfahani DR, Moisak GI, Rzaev JA, Slavin KV: Motor cortex stimulation for deaffe-

rentation pain. *Current Pain and Headache Reports,* 2018, 22:45.
31. Meyerson BA, Lindblom U, Linderoth B, et al: Motor cortex stimulation as treatment of trigeminal neuropathic pain. *Acta Neurochir Suppl,* 1993, 58:150–153.
32. Schrock LE, Mink JW, Woods DW, Porta M, Servello D, Visser-vandewalle V, et al. Tourette Syndrome Deep Brain Stimulation: A Review and Updated Recommendations International Parkinson and Movement Disorder Society Deep brain stimulation is an established treatment Methods An experienced group of physicians participating in. 2015;30(4).
33. H. Rıchard Wınn M. Youmans & Winn Neurological Surgery. *Elsevier Inc*.; 2017. 5720 p.
34. Spiegel EA, Wycis HT, Marks M, Lee AJ. Stereotaxic apparatus for operations on the human brain. *Science*, 1947; 106: 349–350.
35. Valenstein ES. Brain Control. New York: John Wiley and Sons; 1973.
36. Heath RG. Studies in Schizophrenia. A Multidisciplinary Approach to MindBrain Relationships. Cambridge, MA: Harvard University Press; 1954.
37. Pool JL, Clark WD, Hudson P, Lombardo M. Hypothalamic-Hypophyseal Interrelationships. Springfield, Il: Charles C. Thomas; 1956.
38. Heath RG, Mickle WA. Evaluation of seven years' experience with depth electrode studies in human patients. In: Ramey ER, O'Doherty, editors. Electrical Studies on the Unanaesthetized Brain. New York: PB Hoeber; 1960.
39. Richardson DE, Akil H. Pain reduction by electrical brain stimulation in man. Part 1: Acute administration in periaqueductal and periventricular sites. *J Neurosurg,* 1977; 47: 178–183.
40. Boivie J, Meyerson BA. A correlative anatomical and clinical study of pain suppression by deep brain stimulation. *Pain*, 1982; 13: 113–126.
41. Dionne RA, Mueller GP, Young RF, et al. Contrast medium causes the apparent increase in beta-endorphin levels in human cerebrospinal fluid following brain stimulation. *Pain*, 1984; 20: 313–321.
42. Rezai AR, Lozano AM, Crawley AP, et al. Thalamic stimulation and functional magnetic resonance imaging: localization of cortical and subcortical activation with implanted electrodes. Technical note. *J Neurosurg*, 1999; 90: 583–590.
43. Cassinari V, Pagni CA. Central Pain. Cambridge, MA: Harvard University Press; 1969.
44. Garcin R. In: Chan J, Charpentier J, editors. Pain. New York: Academic Press; 1968.
45. 45-Gerhart KD, Yezierski RP, Fang ZR. Inhibition of primate spinothalamic tract neurons by stimulation in ventral posterior lateral (VPLc) thalamic nucleus: possible mechanisms. *J Neurophysiol*, 1983; 49: 406–423.
46. Schofferman,J.,Fishman,S. M., Harden ,R.N., and Kirschner,K.L.(2014). Did we reach too far? The opioid epidemic and chronic pain. PM R 6, 78-84. Doi:10.1016/j.pmrj.2013.12.003.
47. Neurochirurgie S De. Lack of agreement between direct magnetic resonance imaging and statistical determination of a subthalamic target: the role of electrophysiological guidance. 2002;97:591–7. 45.
48. Yelnik J, Damier P, Demeret S, Gervais D, Bardinet E, Bejjani BP, et al. Localization of stimulating electrodes in patients with Parkinson disease by using a threedimensional atlas-magnetic resonance imaging coregistration method. J Neurosurg. 2003;99(1):89–99.
49. Pouratian N. Stereotactic and Functional Neurosurgery Principles and Applications Springer Nature. Springer; 2020.
50. Montgomery, Erwin B. J. Deep Brain Stimulation Programming, Principles and Practice. Oxford Unıversıty Press; 2010.
51. Hariz MI. Complications of deep brain stimulation surgery. *Mov Disord*, 2002;17:S162
52. Beric A, Kelly PJ, Rezai A, et al. Complications of deep brain stimulation surgery. *Stereotact Funct Neurosurg*, 2001;77:73 8.
53. William J.Marks Jr. Deep Brain Stimulation Management-Cambridge University Press. 2011; 1:100-101 .
54. Inci S, Erbengi A, Berker M. Pulmonary embolism in neurosurgical patients. *Surg Neurol*, 1995;43:123 8; discussion 128 9.
55. Voges J, Hilker R, Botzel K, et al. Thirty days complication rate following surgery performed for deep brain stimulation. *Mov Disord*, 2007;22:1486 9.
56. Krack P, Batir A, Van Blercom N, et al. Five year follow up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N Engl J Med*, 2003;349:1925 34.
57. Deep Brain Stimulation for Parkinson's Disease Study Group. Deep brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. *N Engl J Med*, 2001; 345:956 63.
58. Volkmann J, Allert N, Voges J, et al. Safety and efficacy of pallidal or subthalamic nucleus stimulation in advanced PD. *Neurology,* 2001;56:548 51.
59. Okun MS, Tagliati M, Pourfar M, et al. Management of referred deep brain stimulation failures: a retrospective analysis from two movement disorders centers. *Arch Neurol*, 2005;62:1250 5.

60. Ervin FR, Mark VH, Stevens J. İnsanda beyin stimülasyonuna davranışsal ve duygusal tepkiler. *Proc Annu Meet Am* .1969; 58 :54-65.
61. Schvarcz JR. Chronic stimulation of the septal area for the relief of intractable pain. *Appl Neurophysiol.* 1985;48(1–6):191–4.
62. Schvarcz JR. Long-term results of stimulation of the septal area for relief of neurogenic pain. *Acta Neurochir Suppl.*, 1993;58:154–5.
63. Hosobuchi Y, Adams JE, Rutkin B. Chronic thalamic stimulation for the control of facial anesthesia dolorosa. *Arch Neurol.*, 1973;29(3):158–61.
64. Mazars G, Merienne L, Ciolocca C. Intermittent analgesic thalamic stimulation. Preliminary note. *Rev Neurol.,* 1973;128(4):273–9.
65. Mazars G, Merienne L, Cioloca C. Treatment of certain types of pain with implantable thalamic stimulators. *Neurochirurgie,* 1974;20(2):117–24.
66. Turnbull IM, Shulman R, Woodhurst WB. Thalamic stimulation for neuropathic pain. *J Neurosurg.* 1980;52(4):486–93.
67. Hosobuchi Y. Tryptophan reversal of tolerance to analgesia induced by central grey stimulation. *Lancet,* 1978;2(8079):47.
68. Meyerson BA, Boethius J, Carlsson AM. Percutaneous central gray stimulation for cancer pain. *Appl Neurophysiol.*, 1978;41(1–4):57–65.
69. Fields HL, Adams JE. Pain after cortical injury relieved by electrical stimulation of the internal capsule. *Brain,* 1974;97(1):169–78.
70. Adams JE, Hosobuchi Y, Fields HL. Stimulation of internal capsule for relief of chronic pain. *J Neurosurg*, 1974;41(6):740–4.
71. Hosobuchi Y, Adams JE, Rutkin B. Chronic thalamic and internal capsule stimulation for the control of central pain. *Surg Neurol*, 1975;4(1):91–2.
72. Namba S, Nakao Y, Matsumoto Y, et al. Electrical stimulation of the posterior limb of the internal capsule for treatment of thalamic pain. *Appl Neurophysiol.,* 1984;47(3):137–48. [PubMed] [Google Scholar]
73. Namba S, Wani T, Shimizu Y, et al. Sensory and motor responses to deep brain stimulation. Correlation with anatomical structures. *J Neurosurg.* 1985;63(2):224–34.
74. Franzini A, Cordella R, Nazzi V, et al. Long-term chronic stimulation of internal capsule in poststroke pain and spasticity. Case report, long-term results and review of the literature. *Stereotact Funct Neurosurg*. 2008;86(3):179–83. [PubMed] [Google Scholar]
75. Plow EB, Malone DA, Jr, Machado A. Deep brain stimulation of the ventral striatum/anterior limb of the internal capsule in thalamic pain syndrome: study protocol for a pilot randomized controlled trial. *Trials.* 2013;14:241.
76. Boccard SG, Pereira EA, Moir L, et al. Long-term outcomes of deep brain stimulation for neuropathic pain. *Neurosurgery*, 2013;72(2):221–30. discussion: 231.
77. Weigel R, Krauss JK. Center median-parafascicular complex and pain control. Review from a neurosurgical perspective. *Stereotact Funct Neurosurg.* 2004;82(2–3):115–26.
78. Richardson DE, Akil H. Pain reduction by electrical brain stimulation in man. Part 2: chronic self-administration in the periventricular gray matter. *J Neurosurg.* 1977;47(2):184–94.
79. Richardson DE, Akil H. Chronic Self-Administered brain stimulation for the relief of intractable pain.. Paper presented at: 7th Annual Meeting of Neuro Electric. Soc. 1974.; Louisiana. November 21, 1974.
80. Boethius J, Lindblom V, Meyerson BA, et al. Sensory functions of the skin in primates, with special reference to man. Pergamon Press; Oxford (United Kingdom): 1976. Effects of multifocal stimulation on pain and somatosensory functions. pp. 531–48.
81. Hosobuchi Y, Adams JE, Linchitz R. Pain relief by electrical stimulation of the central gray matter in humans and its reversal by naloxone. *Science*. 1977;197(4299):183–6.
82. Hosobuchi Y. Combined electrical stimulation of the periaqueductal gray matter and sensory thalamus. *Appl Neurophysiol.* 1983;46(1–4):112–5.
83. Green AL, Owen SL, Davies P, et al. Deep brain stimulation for neuropathic cephalalgia. *Cephalalgia.* 2006;26(5):561–7.
84. Owen SL, Green AL, Nandi DD, et al. Deep brain stimulation for neuropathic pain. *Acta Neurochir Suppl.* 2007;97(Pt 2):111–6.
85. Green AL, Shad A, Watson R, et al. N-of-1 trials for assessing the efficacy of deep brain stimulation in neuropathic pain. *Neuromodulation.* 2004;7(2):76–81.
86. Bittar RG, Kar-Purkayastha I, Owen SL, et al. Deep brain stimulation for pain relief: a meta-analysis. *J Clin Neurosci.* 2005;12(5):515–9.
87. Owen SL, Heath J, Kringelbach M, et al. Pre-operative DTI and probabilistic tractography in four patients with deep brain stimulation for chronic pain. *J Clin Neurosci.* 2008;15(7):801–5.
88. Franzini A, Ferroli P, Leone M, et al. Hypothalamic deep brain stimulation for the treatment of chronic cluster headaches: a series report. *Neuromodulation.* 2004;7(1):1–8.

89. Fontaine D, Lanteri-Minet M, Ouchchane L, et al. Anatomical location of effective deep brain stimulation electrodes in chronic cluster headache. *Brain.* 2010;133(Pt 4):1214–23.
90. Piacentino M, D'Andrea G, Perini F, et al. Drug-resistant cluster headache: long-term evaluation of pain control by posterior hypothalamic deep-brain stimulation. *World Neurosurg.* 2014;81442(2):e11–5.
91. Katayama Y, Tsubokawa T, Hirayama T, et al. Pain relief following stimulation of the pontomesencephalic parabrachial region in humans: brain sites for nonopiate-mediated pain control. *Appl Neurophysiol.* 1985;48(1–6):195–200.
92. Young RF, Tronnier V, Rinaldi PC. Chronic stimulation of the Kolliker-Fuse nucleus region for relief of intractable pain in humans. *J Neurosurg.* 1992;76(6):979–85.
93. Mallory GW, Abulseoud O, Hwang SC, et al. The nucleus accumbens as a potential target for central poststroke pain. *Mayo Clin Proc.* 2012;87(10):1025–31.
94. Boccard SG, Pereira EA, Moir L, et al. Deep brain stimulation of the anterior cingulate cortex: targeting the affective component of chronic pain. *Neuro-report.* 2014;25(2):83–8.