

BÖLÜM 2

COVID-19'un Santral Sinir Sistemi Üzerine Etkileri ve Nörobilişsel Bozukluklar

Ahmet Alp KARAKAŞLI¹

SARS-CoV-2, 2019'un sonunda, ilk olarak Çin'de görülen bir dizi pnömöni vakasının nedeni olarak tespit edilen yeni bir koronavirüs türüdür. Dünya Sağlık Örgütü SARS-CoV-2'nin neden olduğu hastalığı yeni koronavirüs hastalığı-2019 (COVID-19) olarak isimlendirmiş ve Mart 2020'de pandemi olarak ilan etmiştir.

Hastalığın tanımlanmasından kısa bir süre sonra COVID-19 nedeniyle yatırılan hastaların önemli kısmında santral sinir sistemiyle ilgili belirtiler görülmüştür. COVID-19 hastalarında anksiyeteden, depresyon, bilişsel bozukluklar, baş ağrısı, anozmi, aguzi, senkop, deliryum, ensefalit ve demiyelinizasyona kadar geniş bir yelpazede nörolojik ve psikiyatrik belirtiler bildirilmiştir (1).

¹ Dr. Öğr. Üyesi, Hitit Üniversitesi Tıp Fakültesi, ahmetalpkarakasli@hitit.edu.tr



Kaynaklar

1. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, Sánchez-Larsen Á, Layos-Romero A, García-García J et al. Neurologic manifestations in hospitalized patients with COVID-19: the ALBACOVID registry. *Neurology*. 2020; 95(8): e1060-e1070.
2. Kirtipal N, Bharadwaj S ve Kang SG. From SARS to SARS-CoV-2, insights on structure, pathogenicity and immunity aspects of pandemic human coronaviruses. *Infection, Genetics and Evolution*. 2020; 85: 104502.
3. Li K, Wohlford-Lenane C, Perlman S, Zhao J, Jewell AK, Reznikov LR et al. Middle East respiratory syndrome coronavirus causes multiple organ damage and lethal disease in mice transgenic for human dipeptidyl peptidase 4. *The Journal of infectious diseases*. 2016; 213(5): 712-722.
4. Dong M, Zhang J, Ma X, Tan J, Chen L, Liu S et al. ACE2, TMPRSS2 distribution and extrapulmonary organ injury in patients with COVID-19. *Biomedicine & Pharmacotherapy*. 2020; 131: 110678.
5. Chen R, Wang K, Yu J, Howard D, French L, Chen Z et al. The spatial and cell-type distribution of SARS-CoV-2 receptor ACE2 in the human and mouse brains. *Frontiers in neurology*. 2021; 11: 573095.
6. Tsvigoulis G, Fragkou P, Lachanis S, Palaiodimou L, Lambadiari V, Papatanasidou M et al. Olfactory bulb and mucosa abnormalities in persistent COVID-19 induced anosmia: a Magnetic Resonance Imaging study. *European journal of neurology*. 2020.
7. Matschke J, Lütgehetmann M, Hagel C, Spermhake JP, Schröder AS, Edler C et al. Neuropathology of patients with COVID-19 in Germany: a post-mortem case series. *The Lancet Neurology*. 2020; 19(11): 919-929.
8. Lee M-H, Perl DP, Nair G, Li W, Maric D, Murray H et al. Microvascular injury in the brains of patients with Covid-19. *New England Journal of Medicine*. 2021; 384(5): 481-483.
9. Thakur KT, Miller EH, Glendinning MD, Al-Dalahmah O, Banu MA, Boehme AK et al. COVID-19 neuropathology at columbia university irving medical center/New York presbyterian hospital. *Brain*. 2021; 144(9): 2696-2708.
10. Channappanavar R ve Perlman S. *Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology*. in *Seminars in immunopathology*. 2017. Springer.
11. Liu B, Li M, Zhou Z, Guan X ve Xiang Y. Can we use interleukin-6 (IL-6) blockade for coronavirus disease 2019 (COVID-19)-induced cytokine release syndrome (CRS)? *Journal of autoimmunity*. 2020; 111: 102452.



12. Guerrero JI, Barragán LA, Martínez JD, Montoya JP, Peña A, Sobrino FE et al. Central and peripheral nervous system involvement by COVID-19: a systematic review of the pathophysiology, clinical manifestations, neuropathology, neuroimaging, electrophysiology, and cerebrospinal fluid findings. *BMC infectious diseases*. 2021; 21(1): 1-15.
13. Ye Q, Wang B ve Mao J. The pathogenesis and treatment of the Cytokine Storm in COVID-19. *Journal of infection*. 2020; 80(6): 607-613.
14. Risitano AM, Mastellos DC, Huber-Lang M, Yancopoulos D, Garlanda C, Cicceri F et al. Complement as a target in COVID-19? *Nature Reviews Immunology*. 2020; 20(6): 343-344.
15. Bellon M, Schweblin C, Lambeng N, Cherpillod P, Vazquez J, Lalive PH et al. Cerebrospinal fluid features in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcription polymerase chain reaction (RT-PCR) positive patients. *Clinical Infectious Diseases*. 2021; 73(9): e3102-e3105.
16. Alquisiras-Burgos I, Peralta-Arrieta I, Alonso-Palomares LA, Zacapa-Gomez AE, Salmeron-Barcenas EG ve Aguilera P. Neurological complications associated with the blood-brain barrier damage induced by the inflammatory response during SARS-CoV-2 infection. *Molecular neurobiology*. 2021; 58(2): 520-535.
17. Tremblay M-E, Madore C, Bordeleau M, Tian L ve Verkhratsky A. Neuropathobiology of COVID-19: the role for glia. *Frontiers in Cellular Neuroscience*. 2020; 14: 592214.
18. Dhont S, Derom E, Van Braeckel E, Depuydt P ve Lambrecht BN. Conceptions of the pathophysiology of happy hypoxemia in COVID-19. *Respiratory Research*. 2021; 22(1): 1-3.
19. Engelhardt S, Patkar S ve Ogunshola O. Cell-specific blood-brain barrier regulation in health and disease: a focus on hypoxia. *British journal of pharmacology*. 2014; 171(5): 1210-1230.
20. Erickson MA, Rhea EM, Knopp RC ve Banks WA. Interactions of SARS-CoV-2 with the blood-brain barrier. *International Journal of Molecular Sciences*. 2021; 22(5): 2681.
21. Tian M, Liu W, Li X, Zhao P, Shereen MA, Zhu C et al. HIF-1 α promotes SARS-CoV-2 infection and aggravates inflammatory responses to COVID-19. *Signal Transduction and Targeted Therapy*. 2021; 6(1): 1-13.
22. Cui S, Chen S, Li X, Liu S ve Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis*. 2020; 18(6): 1421-1424.
23. Gu SX, Tyagi T, Jain K, Gu VW, Lee SH, Hwa JM et al. Thrombocytopenia and endotheliopathy: crucial contributors to COVID-19 thromboinflammation. *Nature Reviews Cardiology*. 2021; 18(3): 194-209.



24. Libby P ve Lüscher T. COVID-19 is, in the end, an endothelial disease. *European heart journal*. 2020; 41(32): 3038-3044.
25. Puelles VG, Lütgehetmann M, Lindenmeyer MT, Sperhake JP, Wong MN, Allweiss L et al. Multiorgan and renal tropism of SARS-CoV-2. *New England Journal of Medicine*. 2020; 383(6): 590-592.
26. Sagris D, Papanikolaou A, Kvernland A, Korompoki E, Frontera JA, Troxel AB et al. COVID-19 and ischemic stroke. *European journal of neurology*. 2021; 28(11): 3826-3836.
27. Vasilevska V, Guest PC, Bernstein H-G, Schroeter ML, Geis C ve Steiner J. Molecular mimicry of NMDA receptors may contribute to neuropsychiatric symptoms in severe COVID-19 cases. *Journal of Neuroinflammation*. 2021; 18(1): 1-8.
28. Mehta SK ve Sunder A. Getting paralysed after COVID: Guillain-Barre syndrome. *Journal of Family Medicine and Primary Care*. 2021; 10(7): 2706.
29. Gammazza AM, Légaré S, Bosco GL, Fucarino A, Angileri F, Oliveri M et al. Molecular mimicry in the post-COVID-19 signs and symptoms of neurovegetative disorders? *The Lancet Microbe*. 2021; 2(3): e94.
30. Nersesjan V, Fonsmark L, Christensen RH, Amiri M, Merie C, Lebech A-M et al. Neuropsychiatric and Cognitive Outcomes in Patients 6 Months After COVID-19 Requiring Hospitalization Compared With Matched Control Patients Hospitalized for Non-COVID-19 Illness. *JAMA psychiatry*. 2022; 79(5): 486-497.
31. Alemanno F, Houdayer E, Parma A, Spina A, Del Forno A, Scatolini A et al. COVID-19 cognitive deficits after respiratory assistance in the subacute phase: A COVID-rehabilitation unit experience. *Plos one*. 2021; 16(2): e0246590.
32. Pistarini C, Fiabane E, Houdayer E, Vassallo C, Manera MR ve Alemanno F. Cognitive and emotional disturbances due to COVID-19: an exploratory study in the rehabilitation setting. *Frontiers in Neurology*. 2021: 500.
33. Sahoo S, Suman A, Mehra A, Nehra R, Bhalla A, Puri GD et al. Cognitive Deficits in Patients with COVID-19 Infection during Their Hospital Stay: An Exploratory Study. *Journal of Neurosciences in Rural Practice*. 2022.
34. Ermis U, Rust MI, Bungenberg J, Costa A, Dreher M, Balfanz P et al. Neurological symptoms in COVID-19: a cross-sectional monocentric study of hospitalized patients. *Neurological research and practice*. 2021; 3(1): 1-12.
35. Beaud V, Crottaz-Herbette S, Dunet V, Vaucher J, Bernard-Valnet R, Du Pasquier R et al. Pattern of cognitive deficits in severe COVID-19. *Journal of Neurology, Neurosurgery & Psychiatry*. 2021; 92(5): 567-568.

36. Whiteside DM, Oleynick V, Holker E, Waldron EJ, Porter J ve Kasprzak M. Neurocognitive deficits in severe COVID-19 infection: case series and proposed model. *The Clinical Neuropsychologist*. 2021; 35(4): 799-818.
37. Triana R, Martínez C, Almeida T, González MÁÁ, Vaillant T ve Barreto Y. Cognitive performance in convalescent covid-19 patients. *Revista Cubana de Hematología, Inmunología y Hemoterapia*. 2020: 1-17.
38. Woo MS, Malsy J, Pöttgen J, Seddiq Zai S, Ufer F, Hadjilaou A et al. Frequent neurocognitive deficits after recovery from mild COVID-19. *Brain communications*. 2020; 2(2): fcaa205.
39. Méndez R, Balanzá-Martínez V, Luperdi SC, Estrada I, Latorre A, González-Jiménez P et al. Short-term neuropsychiatric outcomes and quality of life in COVID-19 survivors. *Journal of internal medicine*. 2021; 290(3): 621-631.
40. Miskowiak K, Johnsen S, Sattler S, Nielsen S, Kunalan K, Rungby J et al. Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. *European Neuropsychopharmacology*. 2021; 46: 39-48.
41. Stavem K, Einvik G ve Lundqvist C. *Cognitive impairment 13 months after hospitalization for COVID-19*. in *Open Forum Infectious Diseases*. 2022. Oxford University Press.
42. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV ve Group WCC-DW. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *The Lancet Infectious Diseases*. 2021.
43. Thompson EJ, Williams DM, Walker AJ, Mitchell RE, Niedzwiedz CL, Yang TC et al. Risk factors for long COVID: analyses of 10 longitudinal studies and electronic health records in the UK. *MedRxiv*. 2021.
44. Dennis A, Wamil M, Alberts J, Oben J, Cuthbertson DJ, Wootton D et al. Multiorgan impairment in low-risk individuals with post-COVID-19 syndrome: a prospective, community-based study. *BMJ open*. 2021; 11(3): e048391.
45. World Health Organization, *Mental health and psychosocial considerations during the COVID-19 outbreak, 18 March 2020*. 2020, World Health Organization.
46. Helms J, Kremer S, Merdji H, Schenck M, Severac F, Clere-Jehl R et al. Delirium and encephalopathy in severe COVID-19: a cohort analysis of ICU patients. *Critical Care*. 2020; 24(1): 1-11.
47. Shao S-C, Lai C-C, Chen Y-H, Chen Y-C, Hung M-J ve Liao S-C. Prevalence, incidence and mortality of delirium in patients with COVID-19: a systematic review and meta-analysis. *Age and ageing*. 2021; 50(5): 1445-1453.



48. Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT ve Ely E. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. *Critical care*. 2020; 24(1): 1-9.
49. Hariyanto TI, Putri C, Arisa J, Situmeang RFV ve Kurniawan A. Dementia and outcomes from coronavirus disease 2019 (COVID-19) pneumonia: a systematic review and meta-analysis. *Archives of Gerontology and Geriatrics*. 2021; 93: 104299.
50. Gil R ve Arroyo-Anlló EM. Alzheimer's disease and face masks in times of COVID-19. *Journal of Alzheimer's Disease*. 2021; 79(1): 9-14.
51. Alves VP, Casemiro FG, Araujo BGD, Lima MaDS, Oliveira RSD, Fernandes FTDS et al. Factors associated with mortality among elderly people in the COVID-19 pandemic (SARS-CoV-2): a systematic review and meta-analysis. *International Journal of Environmental Research and Public Health*. 2021; 18(15): 8008.
52. Numbers K ve Brodaty H. The effects of the COVID-19 pandemic on people with dementia. *Nature Reviews Neurology*. 2021; 17(2): 69-70.
53. Bonanad C, García-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-González V, Facila L et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *Journal of the American Medical Directors Association*. 2020; 21(7): 915-918.
54. Kuo C-L, Pilling LC, Atkins JL, Masoli JA, Delgado J, Kuchel GA et al. ApoE e4e4 genotype and mortality with COVID-19 in UK Biobank. *The Journals of Gerontology: Series A*. 2020; 75(9): 1801-1803.
55. Verkhratsky A, Li Q, Melino S, Melino G ve Shi Y. Can COVID-19 pandemic boost the epidemic of neurodegenerative diseases? *Biology direct*. 2020; 15(1): 1-8.
56. Cagnin A, Di Lorenzo R, Marra C, Bonanni L, Cupidi C, Laganà V et al. Behavioral and psychological effects of coronavirus disease-19 quarantine in patients with dementia. *Frontiers in psychiatry*. 2020; 11: 578015.
57. Simonetti A, Pais C, Jones M, Cipriani MC, Janiri D, Monti L et al. Neuropsychiatric symptoms in elderly with dementia during COVID-19 pandemic: definition, treatment, and future directions. *Frontiers in psychiatry*. 2020; 11: 579842.
58. Liu X, Yan W, Lu T, Han Y ve Lu L. Longitudinal Abnormalities in Brain Structure in COVID-19 Patients. *Neuroscience Bulletin*. 2022: 1-5.