

# Sabuncuoglu Serefeddin Health Science (SSHS)

ISSN: 2667-6338, 202-/Vol.3:2

# EFFECT OF MULTIPLE SCLEROSIS ON BRAIN STRUCTURES

# \*1Nihal GÜRLEK ÇELİK, \*2Saadet ERDEM

\*1Kırsehir Ahi Evran University, Faculty of Health Sciences, Department of Nursing, Kırsehir, Turkey

\*2Bolu Abant İzzet Baysal University, Faculty of Health Sciences, Department of Nursing, Bolu, Turkey

Review

Received: 18.08.2021 Accepted: 29.08.2021
\*Corresponding author: nihal.g.celik@gmail.com

# Abstract

In this review, it is aimed to summarize the scientific findings made in recent years about Multiple Sclerosis (MS), whose etiology isn't known exactly, and the anatomy of the brain structures affected by it.

MS is a chronic and neurodegenerative disease of the Central Nervous System, which starts suddenly and insidiously, accompanied by various degrees of inflammation, demyelination and axonal damage. MS is more common between the ages of 20 and 40, and in women. It is stated that the prevalence of MS varies according to ethnic groups and geographical regions. Symptoms of MS vary according to the area of involvement. Some areas where the lesions are generally involved are the optic nerve, periventricular and periaqueductal region, floor of the 4th ventricle, posterior end of the lateral ventricle, centrum semiovale and corpus callosum. In this review the effects of MS in the n. opticus, ventriculus lateralis and corpus callosum will be presented from an anatomical point of view.

**Key Words:** Anatomy, Atrophy, Brain, Multiple Sclerosis

# Özet

Bu derlemede etiyolojisi tam olarak bilinemeyen Multiple Skleroz'un (MS) ve beraberinde etkilenen beyin yapılarının anatomisi hakkında son yıllarda yapılan bilimsel bulguların özetlenmesi amaçlanmıştır.

MS ani ve sinsi başlayan çeşitli derecelerde inflamasyon, demiyelinizasyon ve aksonal hasarların eşlik ettiği Merkezi Sinir Sistemi'nin kronik ve nörodejeneratif bir hastalığıdır. 20 ile 40 yaşları aralığında ve kadınlarda sık görülmektedir. MS'in görülme sıklığının etnik gruplara ve coğrafi bölgelere göre değiştiği belirtilmektedir. MS'in tutulum gösterdiği bölgeye göre belirtileri değişmektedir. Lezyonların genel olarak tutulum gösterdiği bazı alanlar optik sinir, periventriküler ve periakuaduktal bölge, 4. ventrikülün tabanı, lateral ventrikülün arka ucu, centrum semiovale ve corpus callosum'dur. Bu derlemede n. opticus, ventriculus lateralis ve corpus callosum'daki MS'in etkileri anatomik bakış altında sunulacaktır.

Anahtar Kelimeler: Anatomi, Atrofi, Beyin, Multipl Skleroz

## 1. Introduction

Multiple Sclerosis (MS) is an autoimmune disease accompanied by various degrees of inflammation, demyelination and axonal damage (Tench et al., 2005; Sünter et al., 2019). It is a chronic disease of the Central Nervous System (CNS) and its etiology is not known exactly, but environmental and genetic factors are thought to be effective (Trapp et al., 1998; Dyment et al., 2004; Tench et al., 2005; Ramagopalan et al., 2010).

MS is more common between the ages of 20 and 40, and in women (Kidd, 2001). It is stated that the prevalence of MS varies according to ethnic groups and geographical regions. In an epidemiological study, it was reported that the prevalence of the disease is very high in Northern Europe, North America and Canada, but lower in Japan and China. It is also reported that the prevalence of MS, which is rare in tropical regions, increases proportionally with distance from the equator (Kantarcı & Wingerchuk, 2006; Eraksoy & Akman Demir, 2015). In a study by Wallin et al., it was recorded that the number of MS patients was around 2 million in the world while it was 61,408 in Turkey (Wallin et al., 2019).

Believing MS, the etiology of which is not known exactly, is affected by genetic susceptibility and environmental risk factors, chronic infections such as Epstein-Barr virus, spirochetal bacteria, chlamydophila pneumoniae or varicella zoster are also thought to be triggers (Haberland, 2007; Harder et al., 2018). In addition to environmental factors, it is thought that factors such as smoking, climate conditions, exposure to sunlight, exposure to organic solvents and nutritional status play a negative role in the development of MS (Coo & Aronson, 2004; Marrie, 2004; Leray et al., 2016). Another reason is that some large histocompatibility complexes are more common in MS patients compared to the general population. Individuals with HLA-DR2 on chromosome 6 are particularly susceptible to developing MS. It is known that the changes in these areas have effects on the occurrence and course of the disease (Haberland, 2007; Harder et al., 2018).

The most important clinical feature of MS is frequent attacks and remissions (Miller, 2000). The disease has four clinical courses: Relapsing-Remitting MS, Primary Progressive MS, Secondary Progressive MS and Progressive Relapsing MS (Lublin et al., 1996). Affected areas in different anatomical regions cause differences in clinical symptoms and findings (Haberland, 2007).

Depending on the areas of involvement of the CNS in MS, various symptoms such as paresis, spasticity, fatigue, weakness, sensory symptoms, pain, vision problems, coordination disorder, autonomic dysfunction, behavioral changes, and paroxysmal phenomena can be seen (Rohkamm, 2004; Ünal et al., 2018). Although Magnetic Resonance Imaging (MRI) plays a major role in detecting lesions and atrophies in the brain and spinal cord in MS patients (Barkhof, 2002; Bakshi et al., 2008). Oligoclonal band positivity and high immunoglobulin G (IgG) index in the cerebrospinal fluid (CSF) are also essential indicators (Ünal et al., 2018).

Cerebral atrophy is a clinically significant indicator of MS pathology (Ceccarelli et al., 2012). Atrophy that occurs in the early period is very important in clinical disability and cognitive dysfunctions (Riccitelli et al., 2011). Multiple focal areas of demyelination, called lesions in the brain or spinal cord, are the pathological feature of MS. Although the location, number, size and shape of the lesions vary; lesions typically occur in the white matter, but can also be found in grey structures such as the cerebral cortex, thalamus, and basal ganglia. Some areas where the lesions are generally involved are the optic nerve, periventricular and periaqueductal region, floor of the 4th ventricle, lateral ventricle and corpus callosum (Miller, 2000; Evangelou et al., 2000;

Haberland, 2007; Eraksoy & Akman Demir, 2015). In this review the effects of MS in the n. opticus, ventriculus lateralis and corpus callosum will be presented from an anatomical point of view.

*N. opticus:* It is the second of 12 pairs of cranial nerves. It contains only sensory fibers. The fibers of the optic nerve are myelinated central extensions of multipolar ganglion cells located in layer of the pars optica retina. It extends from the retina to the chiasma opticum. After crossing here, it continues as tractus opticus and comes to the thalamus. The fibers coming out of the thalamus terminate in Brodmann areas 17, 18, 19 in the lobus occipitalis. N. opticus is surrounded by dura mater, arachnoid mater and pia mater (Arıncı & Elhan, 2016; Arifoğlu 2019). N. opticus, which is a part of the CNS, is among the structures first affected by MS. Optic neuritis develops as a result of demyelination or inflammation of the n. opticus (Reich et al., 2018). The incidence of optic neuritis at the onset of MS disease is 20% (Ünal et al., 2018). It has been reported that not only monocular vision loss but also different vision problems may occur in optic neuritis (Reich et al., 2018).

Lateral Ventricles: They are the cavities with three extensions and a volume of 7-10 cc in the Hemispherium cerebri. The lateral ventricles of both sides are separated from each other by the septum pellucidum in the middle, which is covered by the ependyma on both sides. The septum pellucidum is made of white and gray matter and is involved in the corpus callosum at the top and the fornix at the bottom. The inner surface of the lateral ventricles is covered with ependymal cells and contains CSF (Gövsa Gökmen, 2003; Arıncı & Elhan, 2016). It has been found out that the volume of the ventriculus lateralis is significantly increased in MS patients compared to healthy individuals (Fox et al., 2000; Lin et al., 2003).

Corpus callosum (CC): The corpus callosum is the largest of the commissural tracts connecting the same centers of the right and left hemispheres. It is responsible for the transfer and coordination of information from one hemisphere to the other hemisphere (Gövsa Gökmen, 2003; Arıncı & Elhan, 2016). CC, which forms the roof of the third ventricle with the lateral ventricles, has a central role for interhemispheric communication (Aboitiz et al., 1992). CC is one of the parts of the brain where MS lesions and atrophies are most common (Coombs et al., 2004; Yaldızlı et al., 2014). Although CC is normally more resistant to age-related changes axonal damage occurs as a result of inflammation and demyelination (Pozzilli et al., 1994; Ozturk et al., 2010). Damage and cognitive dysfunctions in the corpus callosum can also be seen in benign MS (Mesaros et al., 2009). Corpus callosum atrophy is associated with enlargement of the lateral

ventricles and third ventricles as well as with other measurement of brain atrophy (Simon et al., 1999).

# 2. Conclusion

There is no exact treatment for MS. However, the purpose of treatment management is to prevent the risks of attacks and disability that may occur in the individual and to increase the functionality of doing activities of daily living independently (Chiaravalloti & DeLuca, 2008; Sheremata & Tornes, 2013).

## **Conflicts of interest**

The authors declare that there are no potential conflicts of interest relevant to this article.

### References

- Aboitiz, F., Scheibel, A.B., Fisher, R.S., & Zaidel, E. (1992). Fiber composition of the human corpus callosum. *Brain Research*, 11;598(1-2),143-153. doi:10.1016/0006-8993(92)90178-c.
- Arıncı, K., & Elhan, A. (2016). Anatomi (6. Baskı) Ankara: Günes Tıp kitabevleri.
- Arifoğlu, Y. (2019). Her Yönüyle Anatomi (2. Baskı) İstanbul: İstanbul Tıp kitabevleri.
- Bakshi, R., Thompson, A.J., Rocca, M.A., Pelletier, D., Dousset, V., Barkhof, F., Inglese, M., Guttmann, C.R.G., Horsfield, M.A., & Filippi, M. (2008). MRI in multiple sclerosis: current status and future prospects. *Lancet Neurol*, 7,615–25. doi:10.1016/S1474-4422(08)70137-6.
- Barkhof, F. (2002). The clinico-radiological paradox in multiple sclerosis revisited. *Curr Opin Neurol*, 15(3),239-245. doi: 10.1097/00019052-200206000-00003.
- Ceccarelli, A., Bakshi, R., & Neema, M. (2012). MRI in multiple sclerosis: a review of the current literature. *Curr Opin Neurol*, 25(4), 402-409. doi: 10.1097/WCO.0b013e328354f63f.
- Chiaravalloti, N.D. & DeLuca, J. (2008). Cognitive impairment in multiple sclerosis. *Lancet Neurol*, 7(12), 1139–51. doi: 10.1016/S1474-4422(08)70259-X.
- Coo, H., & Aronson, K.J., (2004). A systematic review of several potential non-genetic risk factors for multiple sclerosis. *Neuroepidemiology*, 23(1-2),1–12. doi: 10.1159/000073969.

- Coombs, B.D., Best, A., Brown, M.S., Miller, D.E., Corboy, J., Baier, M., & Simon, J.H. (2004). Multiple sclerosis pathology in the normal and abnormal appearing white matter of the corpus callosum by diffusion tensor imaging. *Mult Scler Journal* Aug;10(4), 392-7. doi:10.1191/1352458504ms1053oa.
- Dyment, D.A., Ebers, G.C., & Sadovnick, A.D. (2004). Genetics of multiple sclerosis. *Lancet Neurol*, Feb;3(2), 104-10.
- Eraksoy, M., & Akman Demir, G. (2015). Merkezi Sinir Sisteminin Miyelin Hastalıkları. In: *Nöroloji* (2. Baskı) (Öge, A.E., Baykan, B., & Zarko Bahar, S. eds.). İstanbul: Nobel Tıp Kitabevleri.
- Evangelou, N., Konz, D., Esiri, M.M., Smith, S., Palace, J., & Matthews, P.M. (2000). Regional axonal loss in the corpus callosum correlates with cerebral white matter lesion volume and distribution in multiple sclerosis. *Brain*, 123,1845-1849. doi:10.1093/brain/123.9.1845.
- Fox, N.C., Jenkins, R., Leary, S.M., Stevenson, V.L., Losseff, N.A., Crum, W.R., Harvey, R.J., Rossor, M.N., Miller, D.H., & Thompson, A.J. (2000). Progressive cerebral atrophy in MS: a serial study using registered, volumetric MRI. *Neurology*, 54(4), 807–12. doi:10.1212/wnl.54.4.807.
- Gövsa Gökmen, F. (2003). Sistematik Anatomi. İzmir: Güven Kitabevi.
- Haberland, C. (2007). Demyelinating Diseases. *In: Clinical Neuropathology Text and Color Atlas* (first ed.) (Percy, C. eds.) New York: Demos Medical Publishing.
- Harder, L., Bobholz, J.A., & MacAllister, W.S. (2018). Multiple Sclerosis. *In: Neuropsychological Conditions Across the Lifespan* (Donders, J., & Hunter, S.J. eds.) Cambridge University Press, 228–243. doi:10.1017/9781316996751.013.
- Kantarcı, O., & Wingerchuk, D. (2006). Epidemiology and natural history of multiple sclerosis: new insights. *Curr Opin Neurol*, 19(3),248–254. doi:10.1097/01.wco.0000227033.47458.82.
- Kidd, P.M. (2001). Multiple sclerosis, an autoimmune inflammatory disease: prospects for its integrative management. *Altern Med Rev*, 6(6), 540-566.
- Leray, E., Moreau, T., Fromont, A., & Edan, G. (2016). Epidemiology of multiple sclerosis. *Revue Neurologique*, 172, 3-13. http://dx.doi.org/10.1016/j.neurol.2015.10.006.

- Lin, X., Blumhardt, L.D., & Constantinescu, C.S. (2003). The relationship of brain and cervical cord volume to disability in clinical subtypes of multiple sclerosis: a three-dimensional MRI study. *Acta Neurol Scand*, 108, 401-406. doi: 10.1046/j.1600-0404.2003.00160.x.
- Lublin, F.D., & Reingold, S.C. (1996). Defining the clinical course of multiple sclerosis: results of an international survey. *Neurology*, 46, 907–911.
- Marrie, R.A. (2004). Environmental risk factors in multiple sclerosis aetiology. *Lancet Neurol*, 3(12), 709–718. doi: 10.1016/S1474-4422(04)00933-0.
- Mesaros, S., Rocca, M.A., Riccitelli, G., Pagani E, Rovaris M, Caputo D, Ghezzi A, Capra R, Bertolotto A, Comi G & Filippi M. (2009). Corpus callosum damage and cognitive dysfunction in benign MS. *Hum Brain Mapp*, 30(8), 2656-2666. doi:10.1002/hbm.20692.
- Miller, J.R. (2000). Demyelinating diseases, multiple sclerosis. In: *Merritt's Neurology*. (10th ed.) (Merritt's, H.H., & Rowland, P. eds.) Lippincott Williams- Wilkins Publishers.
- Ozturk, A., Smith, S.A., Gordon-Lipkin, E.M., Harrison, D.M., Shiee, N., Pham, D.L., Caffo, B.S., Calabresi, P.A., & Reich, D.S. (2010). MRI of the corpus callosum in multiple sclerosis: association with disabiltiy. *Multiple Sclerosis* 16(2), 166-177. doi:10.1177/1352458509353649.
- Pozzilli, C., Bastianello, S., Bozzao, A., Pierallini, A., Giubilei, F., Argentino, C., & Bozzao, L. (1994).

  No differences in corpus callosum size by sex and aging. A quantitative study using magnetic resonance imaging. *J Neuroimaging*, 4(4), 218-21. doi:10.1111/jon199444218.
- Ramagopalan, S.V., Dobson, R., Meier, U.C., & Giovannoni, G. (2010). Multiple sclerosis: risk factors, prodromes, and potential casual pathway. *Lancet Neurol*, 9(7), 727-39. doi:10.1016/S1474-4422(10)70094-6.
- Reich, D.S., Lucchinetti, C.F., & Calabresi, P.A., (2018). Multiple Sclerosis. *N Engl J Med*, 11;378(2), 169-180. doi: 10.1056/NEJMra1401483.
- Riccitelli, G., Rocca, M.A., Pagani, E., Rodegher, M.E., Rossi, P., Falini, A., Comi, G., & Filippi, M. (2011). Cognitive impairment in multiple sclerosis is associated to different patterns of

- gray matter atrophy according to clinical phenotype. *Hum Brain Mapp*, 32(10), 1535-1543. doi:10.1002/hbm.21125.
- Rohkamm, R. (2004). Color Atlas of Neurology (2nd ed) Stuttgart: Thieme.
- Sheremata, W., & Tornes, L. (2013). Multiple Sclerosis and the spinal cord. *Neurol Clin*, 31, 55–77. http://dx.doi.org/10.1016/j.ncl.2012.09.007.
- Simon, J.H., Jacobs, L.D., Campion, M.K., Rudick, R.A., Cookfair, D.L., Herndon, R.M., Richert, J.R., Salazar, A.M., Fischer, J.S., Goodkin, D.E., Simonian, N., Lajaunie, M., Miller, D.E., Wende, K., Martens-Davidson, A., Kinkel, R.P., Munschauer, F.E. 3rd., & Brownscheidle, C.M. (1999). A longitudinal study of brain atrophy in relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group (MSCRG). *Neurology*, 53(1), 139–48. doi:10.1212/wnl.53.1.139.
- Sünter, G., Kılınç, Ö., Berk, A., Akçabey, S., Saldüz, E., Öztürkçü, H., Günal, D.İ., & Agan, K. (2019). Restless Legs Syndrome/Willis-Ekbom Disease in Multiple Sclerosis Patients with Spinal Cord Lesions. *Arch Neuropsychiatry*. https://doi.org/10.29399/npa.23351.
- Tench, C.R., Morgan, P.S., Jaspan, T., Auer, D.P., & Constantinescu, C.S. (2005). Spinal cord imaging in multiple sclerosis. *J Neuroimaging*, 15(4),94S–102S. doi:10.1177/1051228405283292.
- Trapp, B.D., Peterson, J., Ransohoff, R.M., Rudick, R., Mörk, S., & Bö, L. (1998). Axonal transection in the lesions of multiple sclerosis. *N Engl J Med*, 338(5), 278-285. doi:10.1056/nejm199801293380502.
- Ünal, A., Mavioğlu, H., Altunrende, B., Kale İçen, N., & Ergün, U. (2018). Multipl sklerozda tanı ve ayırıcı tanı. In: *Multiple skleroz tanı ve tedavi kılavuzu (2018*) (Efendi, H., & Yandım Kuşcu, D. eds.) İstanbul: Galenos yayınevi.
- GBD 2016 Multiple Sclerosis Collaborators (Wallin, M.T., Culpepper, W.J., Nichols, E., Bhutta, Z.A., Gebrehiwot, T.T., Hay, S.I., Khalil, I.A., Krohn, K.J., Liang, X., Naghavi, M., Mokdad, A.H., Nixon, M.R., Reiner, R.C., Sartorius, B., Smith, M., Topor-Madry, R., Werdecker, A., Vos, T., Feigin, V.L., & Murray, C.J.L.) (2019). Global, regional and national burden of multiple sclerosis 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*, 18, 269–85. doi:10.1016/S1474-4422(18) 30443-5.

Yaldızlı, Ö., Penner, I.K., Frontzek, K., Naegelin, Y., Amann, M., Papadopoulou, A., Sprenger, T., Kuhle, J., Calabrese, P., Radü, E.W., Kappos, L., & Gass, A. (2014). The relationship between total and regional corpus callosum atrophy, cognitive impairment and fatigue in multiple sclerosis patients. *Multiple Sclerosis Journal*, 20(3), 356-364. doi:10.1177/1352458513496880.