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REVIEW

Psychiatric Disorders in Multiple Sclerosis

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Abstract

Multiple sclerosis (MS) is an autoimmune, inflammatory, neurodegenerative disease of the central nervous system, characterised by demyelinisation and axonal damage. The probability of MS patients experiencing psychiatric disorders is much greater than that of the population not diagnosed with MS. The symptoms of MS, the side-effects of pharmacological treatments, family history, and psychosocial factors can cause the possibility of psychiatric disorders developing, such as depression, anxiety, adjustment disorder, psychosis, bipolar mood disorder, chronic stress, and suicidal thoughts. Literature search for original articles and review in the databases, including PubMed, Google scholar and Scopus from 1996 to 2021. Studies suitable for the purpose of this review were selected and reported. The frequency of psychiatric disorders in MS and the radiological findings in these cases were evaluated. Depression has been reported to be the psychiatric disorder with the highest prevalence as a comorbidity in individuals diagnosed with MS. Depression affects an average of 30% of MS patients, which is a rate 2-5-fold higher than in the general population. The presence of additional psychiatric diagnoses has a high prevalence in MS disease, but the majority are overlooked in the diagnosis and treatment process.

Keywords: Anxiety, comorbiditiy, depression, multiple sclerosis, psychiatric disorders

Introduction

Multiple sclerosis (MS) is an autoimmune, inflammatory, neurodegenerative disease of the central nervous system, characterized by demyelination and axonal damage. Approximately 2.8 million people worldwide have been diagnosed with MS, and the highest frequency has been determined in North America, Western Europe, and Australia. MS generally emerges in early adulthood, progresses chronically causing physical, psychological, and cognitive problems, and is the most widely seen neurological disease (1-4).

A very wide range of symptoms may be seen in MS. Findings in MS cases include gait impairment, loss of strength, spasticity, urinary tract disorders, sexual dysfunction, fatigue, psychiatric disorders, and cognitive changes (5,6).

The multidimensional symptomatology of MS is closely linked to disability status, fatigue level, and emotional status. As a result, the quality of life of patients with MS is adversely affected. A previous study stated that the presence of psychiatric findings caused an increase in Expanded Disability Status Scale scores, and there was a two-way effect of psychiatric findings and disability status on each other. The inflammatory process is the key factor in the pathology of MS, and this has been associated with depressive and bipolar mood disorders. An increase in the inflammatory process and neurodegenerative process can trigger depression (7-10).

The probability of patients with MS experiencing psychiatric disorders is much greater than that of the population without MS. The symptoms of MS, side effects of pharmacological treatment, family history, and psychosocial factors can increase the risk of psychiatric disorders development, such as depression, anxiety, adjustment disorder, psychosis, bipolar mood disorder, chronic stress, and suicidal thoughts. In a meta-analysis, which included 44,452 patients with MS and 220,849 healthy controls, the annual incidence was 979/100,000 for depression, 638/100,000 for anxiety, 328/100,000 for bipolar disorder, and 60/100,000 for schizophrenia in patients with MS, which were higher than those in healthy controls (11-14).

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Many studies have supported the view that there could be a connection between psychiatric disorders and lesions detected in certain brain regions based on magnetic resonance imaging (MRI) findings of patients with MS. In a previous study, follow-up MRI of patients with psychiatric problems revealed white matter hyperintensities on T2-weighted images, which are consistent with MS in 0.83% of 2,783 patients. Frontal lobe lesions are accompanied by mania, psychosis, and catatonic episodes in patients with MS, and this finding is supported by previous studies. More frontal lobe pathologies have been determined in patients with MS and depression than in patients with MS without depression (15-18).

Materials and Methods

The literature search for original and review articles in databases, including PubMed, Google Scholar, and Scopus from 1996 to 2021, was conducted. PubMed and Scopus searched for relevanct articles using the following medical topics terms and keywords: "multiple sclerosis", "psychiatric disorders", "depression", "anxiety", "bipolar disorders", "schizophrenia", "obsessive-compulsive disorders". Studies that met the purpose of this review were selected and reported. The frequency of psychiatric disorders in MS and the radiological findings in these cases were evaluated.

Combination of MS and Depression

Depression was reported to have the highest prevalence as a comorbidity in individuals diagnosed with MS. Depression affects an average of 30% of patients with MS, which is two- to fivefold higher than that in the general population. Just as depression may be seen during the clinical course of MS, it may also occur as a side effect of pharmacological treatments.

The chronic structure of MS causing disability and negatively affecting functionality and quality of life may be reasons why depression is seen more widely in patients with MS than in those with other neurological diseases. The World Health Research of the World Health Organization stated that depression seen as a comorbidity with a chronic disease causes a greater disease burden and a higher rate of workforce loss than a chronic disease alone or depression alone. In patients with MS, depression affects their quality of life, fatigue level, cognitive levels, physical disability, and sleep quality. Therefore, to improve these symptoms, psychiatric treatments should be administered to patients with MS and depression (19-22).

Many cross-sectional and longitudinal studies revealed that depression in patients with MS negatively affects quality of life. In a study of 193 patients with MS, a high level of depression was determined to significantly decrease the health-related quality of life in these patients (23-25). It is thought that depression triggers fatigue in patients with MS, and fatigue, which is seen significantly in patients with MS, negatively affects cognitive functions, and this could trigger depressive symptoms. In short, depressive symptoms and fatigue have a reciprocal effect on each other, causing a vicious circle (26).

In a study of 126 patients with MS and 59 healthy controls, a broad-diameter bilateral cortical atrophy was found to affect all brain lobes in patients with MS, and this atrophy could have caused depression (27). Feinstein et al. (28) examined patients with both MS and depression and reported that T1 and T2 lesion volume was greater in the left medial inferior prefrontal cortex, the gray matter volume was lower, and the cerebrospinal fluid volume in the left anterior temporal region was greater (29).

Lower white matter volume, a decrease in uncinate fascicle fractional anisotropy, and lower resting-state functional connectivity between the amygdala and frontal regions have been determined in patients with both MS and depression than in patients with MS not diagnosed with depression.

Combination of MS and Anxiety

Anxiety disorder affects an average of 22% of patients with MS, which is threefold higher than that in the general population. In patients with relapsing-remitting MS, attack, and remission could be a significant cause of anxiety. As anxiety is together with depression and increased physical disability in most cases, it is associated with impaired functionality and accepted as a trigger for an attack (30-32).

In quantitative volumetric MRI studies by Sobanski et al. (33), with voxel-based morphometry, a significant decrease in gray matter volume was found in the right midtemporal gyrus (Brodmann area) (21) in patients with panic disorder compared with healthy controls. Di Legge et al. (34) reported that in patients with a clinically isolated syndrome, no correlation was found between the initial anxiety points and number of Gd+ lesions and the total lesion burden (volume of T2 and T1 lesions) in the first 6 months of clinical follow-up.

In patients with a chronic disorder that significantly disrupts functionality, they may be more predisposed to anxiety and thoughts of death than the healthy population. According to the data of a 60-year longitudinal study, 291 of 1,388 patients with MS died because of MS, and compared with the general population, the life expectancy of patients with MS was 7 years shorter, with an approximately threefold higher mortality rate. In accordance with these data, a poor general health condition is a factor increasing the level of concern about death (35).

Combination of MS and Bipolar Mood Disorder

Bipolar mood disorder is seen in approximately 13% of patients with MS. The etiology of MS and bipolar disorder comorbidity has not yet been fully clarified. A family history of bipolar disorder is a major risk factor for the development of MS and bipolar coexistence. Some studies have supported the genetic transfer of both diseases. Previous studies have also

shown genetic relationships between bipolar mood disorder and MS in the human leukocyte antigen (HLA) *DR2* gene and mitochondrial transcriptomes (36-38).

Some of the pharmacological treatments used in MS treatment may trigger episodes of bipolar mood disorder. Steroid treatment was reported to cause manic attacks, and pharmacological agents such as tizanidine, baclofen, and dantrolene can cause hypomania.

Literature findings related to brain changes associated with bipolar disorder are heterogeneous. While some studies aim to determine the underlying objective biomarkers of this disease such as functional and structural brain abnormalities, the pathophysiology remains uncertain. Lorefice et al. (39) reported no difference in the whole brain, white matter, and cortical gray matter volumes between MS patients with and without comorbid bipolar disorder, but in patients with MS and bipolar disorder, the volumes of the putamen, nucleus accumbens, and pallidus were lower.

Combination of MS and Psychotic Disorder

Psychosis affects approximately 4% of patients with MS, which is two- to threefold higher than that in the general population. Genetic and immunological causes have been the subject of many studies of the relationship between schizophrenia and MS, and studies have reported that immune system disorders seen in the fetal period and early childhood increase the risk of a psychiatric disorder (40,41). Clinically, there are common directions for both diseases. Both diseases are seen more often in young adults, there are periods of remission and exacerbation in the clinical course, and immunologically, the proinflammatory immune status is predominant.

Genome studies have determined serious intersections in certain genes between schizophrenia and MS. Previous studies have reported 21 independent loci with a connection to both schizophrenia and MS, and there has been a focus on the common points of similar HLA alleles in schizophrenia and MS (42,43).

Feinstein et al. (44) reported that the psychotic group of patients with MS tended to have higher total lesion points, especially around periventricular areas, and lesions in areas specifically around the temporal horn were more significant.

Combination of MS and Obsessive-compulsive Disorder

Obsessive-compulsive disorder (OCD) is seen in approximately 31% of MS patients, and the average prevalence in the general population is 2%. Although no definitive information is related to the etiology of OCD, serotonin and brain dysfunction could influence the development of OCD (45-47). The MRI results of patients with OCD without other neurological disease have shown structural and/or functional abnormalities in the frontostriatothalamic circuit, and this could be a marker that a psychiatric disorder could be associated with an organic-based cause. The functional interactions between cortical-cortical and/or cortical-subcortical regions and brain white matter abnormalities in MS may contribute to the pathogenesis of OCD (48,49).

A study reported a decrease in gray matter volume in the frontotemporal cortex, especially in the volume affecting the right inferior frontal gyrus and the inferior and midtemporal gyruses in patients with MS and OCD compared with patients with MS without other psychiatric disorder (50). In a case study, Douzenis et al. (51) reported that OCD symptoms seen after a diagnosis of MS could be linked to MS plaque found in the right parietal white matter (52).

Moreover, many studies have shown that autoimmunity also influence the development of OCD, and this could support the view that autoimmunity affects the occurrence of OCD in patients with MS.

Conclusion

MS is an autoimmune disease that usually emerges in early adulthood, has a course of attacks and remissions but in some cases has a clinically progressive course, can cause disability, and has a serious effect on functionality and quality of life. Comorbid diseases are frequently seen together with MS as a result of progression in the clinical course, that is, it is a cause of disability and a side effect of pharmocological treatments, and as a result of the increased disease burden.

Other psychiatric diagnoses have a high prevalence in MS, but the majority are overlooked in the diagnosis and treatment process. This results in negative outcomes in the clinical course, functionality, and quality of life. During neurological examinations, the decision for diagnosis and treatment methods must be made based on the scores of neuropsychological tests and MRI findings. In a multidisciplinary diagnosis and treatment process, comorbid psychiatric disorders can be diagnosed early. The early determination of psychiatric problems will significantly contribute to the quality of life and prevention of disease progression.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.I., Concept: Y.I., Design: T.K., Data Collection or Processing: Y.I., T.K., Literature Search: Y.I., T.K., Writing: Y.I., T.K.

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References

1. Gustavsen S, Olsson A, Søndergaard HB, Andresen SR, Sørensen PS, Sellebjerg F, Oturai A. The association of selected multiple sclerosis symptoms with disability and quality of life: a large Danish self-report survey. BMC Neurol 2021;21:317.
2. Wiendl H, Gold R, Berger T, Derfuss T, Linker R, Mäurer M, Aktas O, Baum K, Berghoff M, Bittner S, Chan A, Czaplinski A, Deisenhammer F, Di Pauli F, Du Pasquier R, Enzinger C, Fertl E, Gass A, Gehring K, Gobbi C, Goebels N, Guger M, Haghikia A, Hartung HP, Heidenreich F, Hoffmann O, Kallmann B, Kleinschnitz C, Klotz L, Leussink VI, Leutmezer F, Limmroth V, Lünemann JD, Lutterotti A, Meuth SG, Meyding-Lamadé U, Platten M, Rieckmann P, Schmidt S, Tumani H, Weber F, Weber MS, Zettl UK, Ziemssen T, Zipp F; 'Multiple Sclerosis Therapy Consensus Group' (MSTCG). Multiple Sclerosis Therapy Consensus Group (MSTCG): position statement on disease-modifying therapies for multiple sclerosis (white paper). Ther Adv Neurol Disord 2021;14:17562864211039648.
3. GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019;18:459-480.
4. Milo R, Kahana E. Multiple sclerosis: geoepidemiology, genetics and the environment. Autoimmunity reviews 2010;9:A387-A394.
5. Parker LS, Topcu G, De Boos D, das Nair R. The notion of "invisibility" in people's experiences of the symptoms of multiple sclerosis: a systematic meta-synthesis. Disability and rehabilitation 2021;43:3276-3290.
6. Lakin L, Davis BE, Binns CC, Currie KM, Rensel MR. Comprehensive Approach to Management of Multiple Sclerosis: Addressing Invisible Symptoms-A Narrative Review. Neurol Ther 2021;10:75-98.
7. Altamura AC, Buoli M, Pozzoli S. Role of immunological factors in the pathophysiology and diagnosis of bipolar disorder: comparison with schizophrenia. Psychiatry Clin Neurosci 2014;68:21-36.
8. Schmidt S, Jöstingmeyer P. Depression, fatigue and disability are independently associated with quality of life in patients with multiple Sclerosis: Results of a cross-sectional study. Mult Scler Relat Disord 2019;35:262-269.
9. McKay KA, Tremlett H, Fisk JD, Zhang T, Patten SB, Kastrukoff L, Campbell T, Marrie RA; CIHR Team in the Epidemiology and Impact of Comorbidity on Multiple Sclerosis. Psychiatric comorbidity is associated with disability progression in multiple sclerosis. Neurology 2018;90:e1316-e1323.
10. Frischer JM, Bramow S, Dal-Bianco A, Lucchinetti CF, Rauschka H, Schmidbauer M, Laursen H, Sorensen PS, Lassmann H. The relation between inflammation and neurodegeneration in multiple sclerosis brains. Brain 2009;132:1175-1189.
11. Davis BE, Lakin L, Binns CC, Currie KM, Rensel MR. Patient and Provider Insights into the Impact of Multiple Sclerosis on Mental Health: A Narrative Review. Neurol Ther 2021;10:99-119.
12. Silveira C, Guedes R, Maia D, Curral R, Coelho R. Neuropsychiatric Symptoms of Multiple Sclerosis: State of the Art. Psychiatry Investig 2019;16:877-888.
13. Murphy R, O'Donoghue S, Counihan T, McDonald C, Calabresi PA, Ahmed MA, Kaplin A, Hallahan B. Neuropsychiatric syndromes of multiple sclerosis. J Neurol Neurosurg Psychiatry 2017;88:697-708.
14. Jun-O'Connell AH, Butala A, Morales IB, Henninger N, Deligiannidis KM, Byatt N, Ionete C. The Prevalence of Bipolar Disorders and Association With Quality of Life in a Cohort of Patients With Multiple Sclerosis. J Neuropsychiatry Clin Neurosci 2017;29:45-51.
15. Lyoo IK, Seol HY, Byun HS, Renshaw PF. Unsuspected multiple sclerosis in patients with psychiatric disorders: a magnetic resonance imaging study. J Neuropsychiatry Clin Neurosci 1996;8:54-59.
16. Blanc F, Berna F, Fleury M, Lita L, Ruppert E, Ferriby D, Vermersch P, Vidailhet P, de Seze J. Inaugural psychotic events in multiple sclerosis? Rev Neurol (Paris) 2010;166:39-48.
17. Sidhom Y, Ben Djebara M, Hizem Y, Abdelkefi I, Kacem I, Gargouri A, Gouider R. Bipolar disorder and multiple sclerosis: a case series. Behav Neurol 2014;2014:536503.
18. Hotier S, Maltete D, Bourre B, Jegouzo X, Bourgeois V, Guillin O. A manic episode with psychotic features improved by methylprednisolone in a patient with multiple sclerosis. Gen Hosp Psychiatry 2015;37:621.e1-2.
19. Boeschoten RE, Braamse AMJ, Beekman ATF, Cuijpers P, van Oppen P, Dekker J, Uitdehaag BMJ. Prevalence of depression and anxiety in Multiple Sclerosis: A systematic review and meta-analysis. J Neurol Sci 2017;372:331-341.
20. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. Lancet 2007;370:851-858.
21. Julian L, Merluzzi NM, Mohr DC. The relationship among depression, subjective cognitive impairment, and neuropsychological performance in multiple sclerosis. Mult Scler 2007;13:81-86.
22. Marrie RA, Patten SB, Berrigan LI, Tremlett H, Wolfson C, Warren S, Leung S, Fiest KM, McKay KA, Fisk JD; CIHR Team in the Epidemiology and Impact of Comorbidity on Multiple Sclerosis (ECoMS). Diagnoses of depression and anxiety versus current symptoms and quality of life in multiple sclerosis. Int J MS Care 2018;20:76-84.
23. Storm Van's Gravesande K, Blaschek A, Calabrese P, Rostásy K, Huppke P, Kessler J J, Kalbe E, Mall V; MUSICADO Study group. Fatigue and depression predict health-related quality of life in patients with pediatric-onset multiple sclerosis. Mult Scler Relat Disord 2019;36:101368.
24. Nourbakhsh B, Julian L, Waubant E. Fatigue and depression predict quality of life in patients with early multiple sclerosis: a longitudinal study. Eur J Neurol 2016;23:1482-1486.
25. Rodgers S, Manjaly ZM, Calabrese P, Steinemann N, Kaufmann M, Salmen A, Chan A, Kesselring J, Kamm CP, Kuhle J, Zecca C, Gobbi C, von Wyl V, Ajdacic-Gross V. The Effect of Depression on Health-Related Quality of Life Is Mediated by Fatigue in Persons with Multiple Sclerosis. Brain Sci 2021;11:751.
26. Fernández-Muñoz JJ, Cigarán-Méndez M, Navarro-Pardo E, Pérez-de-Heredia-Torres M, Parás-Bravo P, Fernández-de-Las-Peñas C. Is the association between health-related quality of life and fatigue mediated by depression in patients with multiple sclerosis? A Spanish cross-sectional study. BMJ Open 2018;8:e016297.
27. Pravatà E, Rocca MA, Valsasina P, Riccitelli GC, Gobbi C, Comi G, Falini A, Filippi M. Gray matter trophism, cognitive impairment, and depression in patients with multiple sclerosis. Mult Scler 2017;23:1864-1874.
28. Feinstein A, Roy P, Lobaugh N, Feinstein K, O'Connor P, Black S. Structural brain abnormalities in multiple sclerosis patients with major depression. Neurology 2004;62:586-590.
29. van Geest Q, Boeschoten RE, Keijzer MJ, Steenwijk MD, Pouwels PJ, Twisk JW, Smit JH, Uitdehaag BM, Geurts JJ, van Oppen P, Hulst HE. Fronto-limbic disconnection in patients with multiple sclerosis and depression. Mult Scler 2019;25(5):715-726.
30. Podda J, Ponzio M, Messmer Uccelli M, Pedullà L, Bozzoli F, Molinari F, Monti Bragadin M, Battaglia MA, Zaratin P, Brichetto G, Tacchino A. Predictors of clinically significant anxiety in people with multiple sclerosis: A one-year follow-up study. Mult Scler Relat Disord 2020;45:102417.
31. Paparrigopoulos T, Ferentinos P, Kouzoupis A, Koutsis G, Papadimitriou GN. The neuropsychiatry of multiple sclerosis: focus on disorders of mood, affect and behaviour. Int Rev Psychiatry 2010;22:14-21.
32. Silveira C, Guedes R, Maia D, Curral R, Coelho R. Neuropsychiatric Symptoms of Multiple Sclerosis: State of the Art. Psychiatry Investig 2019;16:877-888.
33. Sobanski T, Wagner G, Peikert G, Gruhn U, Schluttig K, Sauer H, Schlösser R. Temporal and right frontal lobe alterations in panic disorder: a quantitative volumetric and voxel-based morphometric MRI study. Psychol Med 2010;40:1879-1886.
34. Di Legge S, Piattella MC, Pozzilli C, Pantano P, Caramia F, Pestalozza IF, Paolillo A, Lenzi GL. Longitudinal evaluation of depression and anxiety in patients with clinically isolated syndrome at high risk of developing early multiple sclerosis. Mult Scler 2003;9:302-306.

35. Lunde HMB, Assmus J, Myhr KM, Bø L, Grytten N. Survival and cause of death in multiple sclerosis: a 60-year longitudinal population study. J Neurol Neurosurg Psychiatry 2017;88:621-625.
36. Minden SL, Feinstein A, Kalb RC, Miller D, Mohr DC, Patten SB, Bever C Jr, Schiffer RB, Gronseth GS, Narayanaswami P; Guideline Development Subcommittee of the American Academy of Neurology. Evidence-based guideline: assessment and management of psychiatric disorders in individuals with MS: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology 2014;82:174-181.
37. Bozikas VP, Anagnostouli MC, Petrikis P, Sitzoglou C, Phokas C, Tsakanikas C, Karavatos A. Familial bipolar disorder and multiple sclerosis: a three-generation HLA family study. Prog Neuropsychopharmacol Biol Psychiatry 2003;27:835-839.
38. Konradi C, Sillivan SE, Clay HB. Mitochondria, oligodendrocytes and inflammation in bipolar disorder: evidence from transcriptome studies points to intriguing parallels with multiple sclerosis. Neurobiol Dis 2012;45:37-47.
39. Lorefice L, Fenu G, Carta E, Frau J, Coghe G, Contu F, Barracciu MA, Carta MG, Cocco E. Bipolar disorders and deep grey matter in multiple sclerosis: A preliminary quantitative MRI study. Mult Scler Relat Disord 2020;46:102564.
40. Marrie RA, Fisk JD, Tremlett H, Wolfson C, Warren S, Tennakoon A, Leung S, Patten SB; CIHR Team in the Epidemiology and Impact of Comorbidity on Multiple Sclerosis. Differences in the burden of psychiatric comorbidity in MS vs the general population. Neurology 2015;85:1972-1979.
41. Bundey S. Genetics and neurology. Elsevier. 2014.
42. Arneth BM. Multiple Sclerosis and Schizophrenia. Int J Mol Sci 2017;18:1760.
43. Carrieri PB, Montella S, Petracca M. Psychiatric onset of multiple sclerosis: description of two cases. J Neuropsychiatry Clin Neurosci. 2011;23:E6.
44. Feinstein A, du Boulay G, Ron MA. Psychotic illness in multiple sclerosis: a clinical and magnetic resonance imaging study. Br J Psychiatry 1992;161:680-685.
45. Martin P. The epidemiology of anxiety disorders: a review. Dialogues Clin Neurosci 2003;5:281-298.
46. Schirmbeck F, Esslinger C, Rausch F, Englisch S, Meyer-Lindenberg A, Zink M. Antiserotonergic antipsychotics are associated with obsessive-compulsive symptoms in schizophrenia. Psychol Med 2011;41:2361-2373.
47. Shimizu E. Seishin shinkeigaku zasshi = Psychiatria et neurologia Japonica. 2011;113:54-59.
48. Radua J, van den Heuvel OA, Surguladze S, Mataix-Cols D. Meta-analytical comparison of voxel-based morphometry studies in obsessive-compulsive disorder vs other anxiety disorders. Arch Gen Psychiatry 2010;67:701-711.
49. Fontenelle LF, Harrison BJ, Yücel M, Pujol J, Fujiwara H, Pantelis C. Is there evidence of brain white-matter abnormalities in obsessive-compulsive disorder?: a narrative review. Top Magn Reson Imaging 2009;20:291-298.
50. Tinelli E, Francia A, Quartuccio EM, Morreale M, Contessa GM, Pascucci S, Sbardella E, Pozzilli C, Pantano P. Structural brain MR imaging changes associated with obsessive-compulsive disorder in patients with multiple sclerosis. AJNR Am J Neuroradiol 2013;34:305-309.
51. Douzenis A, Michalopoulou PG, Voumvourakis C, Typaldou M, Michopoulos I, Lykouras L. Obsessive-compulsive disorder associated with parietal white matter multiple sclerosis plaques. World J Biol Psychiatry 2009;10:956-960.
52. Foroughipour M, Behdani F, Hebrani P, Marvast MN, Esmatinia F, Akhavanrezayat A. Frequency of obsessive-compulsive disorder in patients with multiple sclerosis: A cross-sectional study. J Res Med Sci 2012;17:248-253.