Review article

Is There a Relation between Brain MRI Active Plaques and Cognitive Disorders in Multiple Sclerosis?

Farshad Gharehbakhshi[1], Golmis Abdolmohammadi[2], Pegah Moharrami Yeganeh[3*], Mehdi Mirzaei[4] Farzaneh Alvandi[5], Ehsan Karimi Behnag[6]

1. Department of Radiology, School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran. **Orcid:** 0000-0001-5495-609X
2. Department of Radiology, School of Medicine, Army University of Medical Science, Tehran, Iran. **Orcid:** 0000-0001-9231-408X
3. School of Medicine Zanjan University of Medical Science, Zanjan, Iran. **Orcid:** 0000-0001-8146-6969
4. Department of Radiology, School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran. **Orcid:** 0009-0006-0342-5532
5. School of Medicen, Zanjan University of Medical Sciences, Zanjan, Iran. **Orcid:** 0009-0003-1076-2148
6. Department of Radiology, School of medicine, Shahid Beheshti university of Medical science, Tehran, Iran. **Orcid:** 0009-0000-9848-9171

***Corresponding Author: Pegah Moharrami Yeganeh.** School of Medicine Zanjan University of Medical Science, Zanjan, Iran. **Email:** p.yeganeh@zums.ac.ir.

Abstract

Mood disorders could be frequently observed in multiple sclerosis (MS) patients. Mood disorders are common condition in multiple sclerosis with high prevalence rates, for example annually prevalence rate of depression is as high as 20% and lifetime prevalence rates is 50%. In addition it observed that bipolar disoder and other cognitive disorders were common in these patients. However, the comorbidity of psychiatric problems and amont of brain damage is not clear. Therfore, this study aimed to investigate the correlation between the active plaques of MS cases' brain MRI and co-occurrence of different cognitive disorders in the same patients. This literature review project was designed based on standard guidelines to evaluate the related data about brain MRI active plaques and cognitive disorders in multiple sclerosis. The study words, which were combined with each other, were “Mood Disorders”, “Active Plaques”, “Multiple Sclerosis”, “MRI”, “Depression”, “Cognitive disorders”, and “Bipolar Disorder”, the data were extracted and compared. The evaluated studies have represented that there is a correlation between depression and the amount of active plaques on the anterior parietal and left temporal area of the MS patients.

Key words: Multiple Sclerosis, Active Plaques, MRI, Cognitive disorders, Mood Disorders, Depression, and Bipolar Disorder.

Submitted: 13 Sep 2024 Revised: 17 Oct 2024 Accepted: 29 Nov 2024

[Downloaded from mail.intjmi.com on 2026-11-19]

Introduction

Multiple Sclerosis (MS) as an autoimmune and chronic, inflammatory disease of Central Nervous System (CNS), is the most common chronic disabling condition of CNS in young adults, which affecting 2.3 million cases worldwide, and is two times more common in female gender rather than in males, in addition its onset is often at young case, around 30 years of age (1, 2). The MS course is unpredictable and variable. Based on the National Multiple Sclerosis Society, there are 4 MS types: Relapsing-remitting MS (RRMS), clinically isolated syndrome (CIS), Secondary progressive MS (SPMS), and Primary progressive MS (PPMS) (3). CIS as the first episode of neurologic symptoms induced by the demyelination and inflammation of CNS, for at least one day (24 hours), which not have the MS criteria. RRMS characterized by the defined attacks occurrence (exacerbations/relapses) of increasing or new neurologic sign and symptoms, which is followed by periods of complete or partial remissions (4). Of note, during periods of remission, the progression of the disease should not be apparent (5). At diagnosis period, proximally 85% of cases had this MS type. Moreover, 80% of RRMS cases will transition to a SPMS, with a progressive and gradual worsening of neurologic function over time (2, 6). If this progressive condition occurs in illness onset, without early remissions or relapses, MS case develops to PPMS, which contains 10% of cases (3, 5). Symptoms of MS include visual acuity loss, muscle weakness, fatigue, sphincter incontinence, anxiety, cognitive deficits, and depression, which may be observed in MS cases. After diagnosis of MS patients, different emotional reactions may be observed, including anxiety, shock, sadness, fear, anger, or sorrow. In this condition, physicians should adopt an empathic, supportive attitude towards the patient (7). So, the relationship between patient and doctor improves when physicians recognize the patient's concerns and respond to them empathetically (8, 9). The psychiatric symptoms presence in MS has been known since Charcot mentioned first description of clinic-pathological of disseminated sclerosis in a lecture at Salpetriere hospital in the 19th century (10). Among psychiatric clinical manifestations mentioned by Charcot were weeping and pathological laughing, mania, euphoria, depression, and hallucinations (11). Indeed, Charcot's patient Mademoiselle V was described as experiencing a fit of severe depression, in addition to paranoia and hallucinations (12). Anyway, the experimental research about the depression prevalence in patients with MS have begun since 1950s (5). In addition to neurological manifestations which can characterize MS, depression as a related condition is common in these patients, with lifetime prevalence as 50 percent (13). While it has historically been difficult to distinguish the direct effects of mood disorders from the nonspecific effects of chronic illness, a recent study shows that the annual prevalence of major depression in MS is higher than in healthy and chronic cases (14, 15). In a study by Patten et al. it was reported as a one year prevalence rate of 25.7% for depression in patients with MS in 18 to 45 years range of age (16). Moreover, it is important to note that the suicidal idea is common in MS cases, and depression in MS cases is often not diagnosed and controlled. Also, depression as an important index of quality of life (QoL) determination in MS may be as most important factor for this condition (1). Therefore, multiple sclerosis may be associated to some different mood disorders, included as depression, bipolar disorder, dysthymia. Therefore, the aim of the current study is to evaluate the association of the brain MRI active plaques and depression in multiple sclerosis, as a literature review study.

[Downloaded from mail.intjmi.com on 2026-11-19]

Patients and Methods

Study setting

This study was approved and conducted in University of Shahid Beheshti of medical science

Study design and search terms

This literature review project was designed based on the standard guidelines to evaluate the related data in relation to depression and multiple sclerosis. The study key words, which were combined with each other, were Multiple Sclerosis, Active Plaques, MRI, Cognitive disorders, Mood Disorders, Depression, and bipolar disorder.

Inclusion and exclusion criteria

Published studies about depression and multiple sclerosis, were evaluated. Furthermore, in this research, review articles and case reports, the studies which have only abstract, examinations which have not safety, book chapter, article not found, abstract of congress, articles that have not statistical indices, inadequate data, or irrelevant were excluded.

Assessment of quality and extraction of data

In research and review studies extracted data were abstracted independently, in addition the following data were extracted: region, country, study period, publication year, size of study sample, study name, and preventive methods of mortality. In addition, study quality was evaluated independently based on Joanna Briggs Institute's critical appraisal checklist. This method includes nine items which is rated as either yes, no, not clear, or not applicable

Databases

The study was carried out in English databases that these sites included as WHO, NHS, Google Scholar, PubMed, Scopus, and Science Direct.

Results

Prevalence of Depression in MS

Major depression or unipolar depression as a mood disorder, characterized by presence five of following clinical manifestations for at least 2 weeks: a bad condition of mood for most days, loss of pleasure or interest in ordinary activities, decreased or increased appetite and weight, sleep disorders, psychomotor agitation or retardation, fatigue, smelling of self-blame and guilt, suicidal thinking and reduced concentration, and negative self-image (2, 19, 20)

The five clinical manifestations include depressed mood, sad, and loss of interest/pleasure in usual actions (21). A recently Australian investigation reported a one year prevalence rate of major depression in community as 6.3% (22). In a 1990 review of affective disorders in MS, Schiffer, et al mentioned that the most investigations had showed a higher prevalence and incidence of depressive symptoms in controls in comparison to patients affected to MS with a different neurological illness. However, it was also mentioned that all these investigations had been designed weaknesses of varying degrees. Specially, Schiffer, et al represented that in the most of studies the physicians diagnosing depression were not blind to condition patient (23).

Minden, et al. evaluated fifteen cases with MS and standardized rating scales for depression (24), they also mentioned that 54% of size sample have research diagnostic criteria (RDC) for depression. In another study, Joffe, et al. evaluated 100 consecutive cases in Canada evaluated by RDC for major depression and reported a life span prevalence rate as 42% (25). Moreover, Sadovnick, et al. which has interviewed 221 cases attending in MS clinic in Vancouver, have evaluated a prevalence as 50% (26). They also have mentioned that this correlation was considerably higher than the depression rates, which reported for chronic illness samples.

Furthermore, Chwastiak, et al. have evaluated 1374 cases of MS with 739 responses (a 54% response rate) (27). They observed that 42% of samples had clinically significant depressive

[Downloaded from mail.intjmi.com on 2026-11-19]

symptoms according to the Centre for Epidemiological Studies' Depression Scale (CES-D) and 29% scored in the moderate or severe range. In another study, Patten et al. have provided a perspective study about the relationship between MS and major depression based on the Canadian Community Health Survey (CCHS) data. They evaluated 115 071 cases, aged 18 years or older, and found 322 MS cases. The one-year depression prevalence was 25.7% compared with 8.9% for normal population. However, studies have mentioned that depression prevalence in MS is higher than other groups with a chronic illness (20).

Depression—be it a formal diagnosis based on consensus clinical criteria, or a collection of Symptoms revealed by a self-report rating scale—is common in patients with multiple sclerosis (MS) and adds substantially to the morbidity and mortality associated with this disease. This Review discusses the prevalence and epidemiology of depression in patients with MS, before covering etiological factors, including genetics, brain pathology, immunological changes, dysregulation of the hypothalamic–pituitary–adrenal axis, and psychosocial influences. Treatment options such as antidepressant drugs, cognitive–behavioral therapy, mindfulness-based therapy, exercise and electroconvulsive therapy are also reviewed in the context of MS-related depression. Frequent comorbid conditions, namely pain, fatigue, anxiety, cognitive dysfunction and alcohol use, are also summarized. The article then explores three key challenges facing researchers and clinicians: what is the optimal way to define depression in the context of diseases such as MS, in which the psychiatric and neurological symptoms overlap; how can current knowledge about the biological and psychological underpinnings of MS-related depression be used to boost the validity of this construct; and can intervention be made more effective through use of combination therapies with additive or synergistic effects, which might exceed the modest benefits derived from their individual components(20)

MS and MRI cognitive findings in patients using Montreal

Among MRI indices only severity of atrophy showed a significant difference between cognitively impaired and cognitively preserved patients .third ventricular volume was significantly correlated with total MoCA score (75).

MS and MRI Pulse sequence in order to better detection of MS lesions in cognitive dysfunction

Although large plaques may visible in all images but important problem in patient with cognitive dysfunctions with suspected MS in screening the tiny MS plaques .this study showed that for revealing the MS plaques located in the subcortical and infratentorial areas, PDw-fat sat is most effective(74).

MS and Suicide

Fatigue and poor sleep quality are among the most common patient-reported problems associated with multiple sclerosis (MS). Social support, on the other hand, is often found to be positively associated with quality of life in patients with neurological diseases. Studies also show that suicidal ideation (SI) levels in MS are elevated compared to the general population. Thus, the aim of this study is to assess the associations between fatigue, social support, and SI in patients with MS. Out of 184 MS patients asked to participate in this cross-sectional study, 156 agreed (RR 69.8%; 75% female; mean age: 39.95 ± 9.97 years). Patients filled-in the Multidimensional Fatigue Inventory-20, the Pittsburgh Sleep Quality Index, the Multidimensional Scale of Perceived Social Support and the subscale of the General Health Questionnaire-28 focused on assessing SI. Models were controlled for age, gender, disease duration, functional disability, and sleep quality. Data were analyzed using multiple linear regressions. SI was positively

[Downloaded from mail.intjmi.com on 2026-11-19]

associated with lower sleep quality and four types of fatigue: general, mental, reduced activity, and reduced motivation ($p < 0.05$). Physical fatigue was not significantly associated with SI. Social support was negatively associated with SI in all models. The final models under study explained from 24.3 to 29.7% of the total variance in SI. SI yielded associations with both sleep quality and fatigue, with the exception of physical fatigue. Information provided by physicians on sleep management, and a psychosocial intervention focused on people who provide support for patients with MS (family, friends, and significant others) may reduce levels of SI.

Mortality rates are elevated in people with multiple sclerosis (MS) relative to the general popu- lation. There is, however, some uncertainty whether suicide contributes to this. Epidemiological data suggest that the standardized mortality ratio (SMR) for suicide in MS is approximately twice that of the general population with younger males in the first few years following diagnosis most at risk. Rates of suicidal intent, a potential harbinger of more self-destructive behavior, are also elevated, but the fre- quency with which intent is followed by suicide is not known. Depression, severity of depression, social isolation, and alcohol abuse are associated with thoughts of suicide. The variables linked with suicide and suicidal intent are therefore well defined and should be readily available from routine clinical inquiry.

While vigilance on the part of clinicians is required, particularly in the context of high-risk patients, it is also recognized that prevention is dependent on full disclosure of intent.

High depression prevalence rates in MS cases raise the probable risk of suicide in this patients. Sadovnick et al. analyzed the death etiologies in a large sample size of cases at 2 Canadian MS clinics (26). The sample of both clinics comprised, 3126 cases and a total of 145 mortalities observed in time period (28). The death etiologies can be clearly established from 119 cases records of whom 56 deaths were records as a direct complication result of MS. Out of 63 cases, which deaths were not as a MS complications result, 18 cases (28.6%) died following the suicide condition. Another two cases whose deaths were as a result of miscellaneous causes' were suspected suicides (3). However, authors have mentioned that the proportion of suicides in MS patients was 7.5 times higher than age-matched general population.

A Danish study evaluated the suicide prevalence in MS cases. They observed that a total of 53 suicides were detected over this time. They mentioned that risk of suicide was higher among the male and younger cases (12). In a recent investigation, Feinstein, et al evaluated 140 cases with MS in Canada by standardized measures to diagnosing suicidal intent and idea. In this study they have been observed a lifetime prevalence rate of suicidal idea as 40 cases (28.6%) and 9 cases (6.4%) had suicide attempt (29).

Brain Lesion Locations

Association of plaque location and depression in MS is under spotlight recently. This relation is important for treating and diagnosing major depression in MS cases. In addition, it could be substantial for developing a complex correlation between psychosocial and biological factors in depression genesis (30). In a recent study, Rabins, et al. evaluated the computed tomography (CT) scans of 37 cases with MS and psychiatric symptoms of them were investigated longitudinally (31). They showed that MS cases with brain plaque were more depressed than the cases by just spinal cord lesions.

Honer, et al compared the magnetic resonance imaging (MRI) of eight matched control MS cases and eight MS cases with psychiatric disorders. They have observed that psychiatric disorders correlated with temporal lobe plaques (32). Another study by Logsdail and Ron have

[Downloaded from mail.intjmi.com on 2026-11-19]

compared the psychiatric morbidity rate in a sample containing 116 MS cases and control group with the physical disabilities (33). Consequently, they observed a significantly higher rate of psychiatric disorder in MS group. Indeed, this study has also mentioned that the depression was associated with greater pathology in temporal parietal area. In addition, Pujol, et al evaluated 45 cases with MS in Barcelona and investigated the correlation between scores on the Beck Depression Inventory (BDI) and location and size of the lesions (34). Zorzon, et al. evaluated 95 cases with MS, they used the Hamilton Rating Scales for Depression. Of their 95 cases, 18 cases (19%) have major depression criteria (35). The authors mentioned that depression severity have a correlation with right frontal lesion and with right temporal brain volume. Eventually, according to the mentioned studies, there are an association between depressions in MS with the neuropathology in the left anterior temporal/parietal regions. But furthermore researches would be required.

Depression and Cognitive Impairment in MS

Cognitive decline is recognized as a prevalent and debilitating symptom of multiple sclerosis (MS), especially deficits in episodic memory and processing speed. The field aims to (1) incorporate cognitive assessment into standard clinical care and clinical trials, (2) utilize state-of-the-art neuroimaging to more thoroughly understand neural bases of cognitive deficits, and (3) develop effective, evidence-based, clinically feasible interventions to prevent or treat cognitive dysfunction, which are lacking. There are obstacles to these goals. Our group of MS researchers and clinicians with varied expertise took stock of the current state of the field, and we identify several important practical and theoretical challenges, including key knowledge gaps and methodologic limitations related to (1) understanding and measurement of cognitive deficits, (2) neuroimaging of neural bases and correlates of deficits, and (3) development of effective treatments. This is not a comprehensive review of the extensive literature, but instead a statement of guidelines and priorities for the field. For instance, we provide recommendations for improving the scientific basis and methodologic rigor for cognitive rehabilitation research. Toward this end, we call for multidisciplinary collaborations toward development of biologically based theoretical models of cognition capable of empirical validation and evidence-based refinement, providing the scientific context for effective treatment discovery

Cognitive impairment is increasingly recognized to be a core feature of multiple sclerosis (MS), with important implications for the everyday life of individuals with MS and for disease management. Unfortunately, the exact mechanisms that underlie this cognitive impairment are poorly understood and there are no effective therapeutic options for this aspect of the disease. During MS, focal brain inflammatory lesions, together with pathological changes of both CNS grey matter and normal-appearing white matter, can interfere with cognitive functions. Moreover, inflammation may alter the crosstalk between the immune and the nervous systems, modulating the induction of synaptic plasticity and neurotransmission. In this Review, we examine the CNS structures and cognitive domains that are affected by the disease, with a specific focus on hippocampal involvement in MS and experimental autoimmune encephalomyelitis, an experimental model of MS. We also discuss the hypothesis that, during MS, immune-mediated alterations of synapses' ability to express long-term plastic changes may contribute to the pathogenesis of cognitive impairment by interfering with the dynamics of neuronal networks

Several studies have reported high rates of depression in multiple sclerosis (MS) with a

[Downloaded from mail.intjmi.com on 2026-11-19]

lifetime prevalence of ~50% and an annual prevalence of 20% not uncommon. Concern about the potential of new drug treatments to exacerbate or precipitate depression in MS has led to increased interest in the relation between MS and depression. This review on MS and depression identifies the following key issues: How common is depression in people with MS? Is depression in MS associated with lesions in specific regions of the central nervous system? Is there an increased risk of suicide in MS? Is there a higher than expected incidence of anxiety disorders in MS? Are fatigue and depressed mood related in MS? Is there a relation between depression and cognitive impairment in MS? Which psychosocial variables affect the development of depression in MS? Does treatment with interferon increase the risk of depression? How effective are treatments for MS patients with depression? Each of these issues is briefly reviewed with critical commentary, and some priorities for future research are suggested.

There are some evidences that cognitive disorders are common in MS with the prevalence rates of 40% or higher (36, 37). A British study which was contained 200 MS cases reported that 46% of the patients had cognitive impairments. Moreover, Rao, et al. have represented that the pattern and the degree of cognitive disorders are highly correlated with the location and the amount of white-matter lesions (38). Additionally, cognitive dysfunction is now well documented in depression; however, the cognitive impairment might be occurred in middle and older aged cases with a severe depression history. Of note, some investigations have shown that there are not any correlation between depression and cognitive dysfunction in MS cases (39). If healthy cases are prone to the cognitive disorders, it seems paradoxical that they are not suitable control case for comparing the depression rate occurrence with the MS patients (40). In a study by Arnett, et al. it has been suggested that MS patients are more likely to be compromised in depression (41). The other research by Demaree, et al. have supported the same results (42, 43); They have represented that there is an association between cognitive dysfunction and depression, and this relation was better appeared in severe depression cases. Moreover, Arnett, et al. have demonstrated that the cognitive dysfunction in MS cases is correlated with negative self-evaluations (44). However, recent studies failed to find clear association between cognitive dysfunction and depression in MS cases.

Depression and Anxiety in MS

Anxiety symptoms and anxiety disorders are prevalent and burdensome, yet poorly managed in multiple sclerosis (MS). Indeed, anxiety disorders occur in 22% of people with MS, and anxiety can negatively impact physical function, cognition, and quality of life. Currently, there are no treatment guidelines available for anxiety in MS, based on limited information regarding the efficacy of pharmacotherapy and psychotherapy. Exercise training may be a promising avenue for treatment of anxiety in MS, and this is based, in part, on a wealth of evidence in the general population of adults. This review provides an overview of anxiety and evidence from meta-analyses and systematic reviews for current treatments options in the general population and MS. We further make a case for exercise as a novel treatment approach that requires focal examination in persons with MS.

Among individuals with multiple sclerosis (MS), mental health comorbidities play a significant role in contributing to secondary disability and detracting from quality of life. This review examines current evidence surrounding three mental health issues of particular relevance to MS: depression, anxiety, and bipolar disorder. We review what is known of the prevalence, correlates, screening mechanisms, and current treatment

[Downloaded from mail.intjmi.com on 2026-11-19]

of each issue and provide recommendations for future areas of research

Of note, the high comorbidity rate in mood disorders and anxiety suggesting that anxiety disorders would be more common in MS patients. A recent review study have assessed the emotional disorders occurrence in MS cases; only 5 of the 15 studies had included a standardized anxiety measure (45). However, these studies have specifically evaluated anxiety and have typically mentioned high rates. In a study by Smith et al. determined the prevalence of depression and anxiety of 88 cases with MS based on BDI criteria (46), and they have mentioned 34% scored as cases for anxiety with 22 cases (25%) which required treatment in this condition. Indeed, some studies have shown the higher anxiety levels in MS cases. However, these investigations evaluated the cases that were employed attending clinics. Thus, the participant patients have higher levels of clinical manifestations than a community-based MS cases.

Findings suggest that attention to anxiety be given as much as depression as it plays a large role in individuals' perceived health and well-being, which subsequently impacts the severity of symptoms and overall quality of life. Early identification of anxiety and potential substance use and increased social support also appear to be crucial for mitigating the impact of depression and anxiety.

Depression and related Fatigue in MS

Fatigue as a common symptom could be observed in both MS and depression. Consequently, it is a challenge for researchers and clinicians to find the correlation between fatigue, depression, and MS. Mohr, et al. have represented that there is An association between depression and fatigue, and MS (10). In addition, two studies represented that fatigue in MS was not occurred concomitantly with depression. Krupp, et al. in another study compared 32 MS cases and healthy ones (47). They observed 47% of MS cases which had clinical depression. In the following, they have not found any statistically significant relation to fatigue in the same patients. Another study have reported no relation between fatigue and depression in systemic lupus erythematosus or MS cases (48). In addition, the study conducted by Vercoulen, et al. represented that fatigue was a troubling symptom in MS cases; but they observed that there is no relation to disability (EDSS) or depression (BDI) (49). A recent study reported a significant relation between fatigue and depression in MS cases which was an psychosocial investigation in 139 American MS cases indeed, the other study by Ford, et al. examined the depression and fatigue in 78 MS cases and found significant relation between mood level and fatigue (51). Furthermore, one longitudinal study observed that the correlation was dynamic (52). Another data was established that fatigue and depression were independent predictors of QoL in MS (15). Moreover, fatigue is well recognized as a clinical manifest of accompanying anxiety and depression (53).

Depression Treatment in MS Cases

There are some growing studies about the treatment of depression in MS cases. Schiffer, et al. in a controlled trial and double blind study administrated antidepressants in depression treatment in MS cases (23), they observed that desipramine comparing a placebo were more effective whereas some cases shown side effects of anticholinergic. Thus, the limited dosage of these drugs would be required. Interestingly, significant improvements were observed according to the clinical judgement and the Hamilton Rating Scale for Depression but not on the BDI (54). Mohr, et al. in a meta-analysis, concluded that depressed MS cases responded well to treatment with either psychotherapy or antidepressants, but demonstrated that psychotherapy with an emphasis on coping skills was more likely to be effective than insight-oriented therapy (55). The same study has reported that both

[Downloaded from mail.intjmi.com on 2026-11-19]

sertraline and CBT were more effective in depression treatment in MS cases compared to supportive-expressive group therapy (55). However, there are some studies indicating that depression in MS cases responds to two psychotherapy and drugs which emphasizes on active coping skills development (54).

Discussion

It was represented that there is a correlation between MS and high prevalence of mood and emotional disorders. Mood disorders can be worsened in the progression of illness and influenced on Qol in patients with MS and their families. In addition, MS is associated with depression, poor treatment adherence, suicide risk, reduced Qol, and function (56). The diagnosis and treatment of the mood and emotional disorders in these cases is often challenging since several clinical manifestations of these mental disorders overlap with MS (57). Other high prevalent mood disorders in MS included as anxiety disorders, emotional blunting (apathy), pseudobulbar affect, and bipolar disorder (20). Early diagnosis and control of these conditions would contribute to reduce the disability and mortality rate (2, 26).

Based on the evaluated studies, mood disorders as a common condition in multiple sclerosis with high prevalence rates. Some other documents mentioned that there are some possibly reason that multiple sclerosis cases could have an increased suicide risk and this possibly more common in male younger cases and these cases could be severely depressed, socially isolated, and alcohol dependences. Carta, et al. in a study in 2014, have mentioned that interaction of two condition (multiple sclerosis and depression) can significantly worsen the clinical outcomes in long-term; actually, impairment and disability of Qol are reinforced in depression cases co-occurrence (3). It should be intended that depression comorbidity probably can be affect the GM, which injury have association with cognitive disorders and disability in MS (28, 58). On the contrary, Womer et al. mentioned that there are not significant correlation between depression and the umbens nucleus volume, but there are significant relationship with the volume of globus pallidus (4); which has negatively relation to the presence of psychotic features. In addition, some studies have demonstrated that the volume of putamen as a possible marker of structural neural of neurodegenerative and neuropsychiatric disorders (7). Indeed. depressive cases, showed significantly smaller putamen size (59), while depression in addition to other psychiatric disorders represented a relation to larger putamen size and hyperdopaminergic states (7, 60). In addition, Rimol, et al. and Hibar, et al. measured that there are significantly lower bilateral thalamus mean volumes in depression (61, 62), determining its role in executive behavior and emotive processing (63).

The association between functional alterations and depression of the deep GM is very intriguing, partially unexplored and complex. Several studies have indicated prefrontal-limbic subcortical and frontal-subcortical regions as a reason of depression development (21), whereas more recent idea mentioned that basal ganglia play an specific role in depression development. It is interesting that nucleus accumbens role has been recently evaluate as a key point for mood disorders, and this condition defined as an interface between action, cognition, emotion, and being a critical node for intrinsic efferent and afferent signals to pallidus and other cGM and scGM conditions (64). The longevity risk of major depression has been estimated as 50% in patients with MS (26, 65), which can be compared with major depression risk in the general population as 10–15% of evaluated cases (66). Based on the high prevalence of this condition, patients' well-being and quality of life importance (67), correlation with suicidality (68), and possible effect on MS

[Downloaded from mail.intjmi.com on 2026-11-19]

course (69-72), depression in MS has been extensively studied. However, several focused and brief studies have been conducted (6, 56). Moreover, a practical consensus statement on depression (73) in some recent years, no review and comprehensive model of relationship between MS and depression has been published. Based on mentioned discussion, there are some relations between depression and active plaques in patients with multiple sclerosis, also in present study we have emphasized on this correlation.

Conclusion

Mood disorders as a common condition in multiple sclerosis with high prevalence rates, for example annually prevalence rates of depression are as high as 20% and lifetime prevalence rates of 50%. In evaluated studies there are some different evidences that depression in multiple sclerosis have a relation link with more active plaques in the anterior parietal / left temporal area, however there are not strong evidence for a link between mood disorders and lesion site. Additionally, some other documents mentioned that there are some possibly reason that multiple sclerosis cases could have an increased suicide risk and this possibility is more common in male younger cases and these cases could be severely depressed, socially isolated, and alcohol dependence. In some other studies, we observed that anxiety disorders, could be more usual in multiple sclerosis. The earlier studies on depression and fatigue in multiple sclerosis consistently not found obvious correlation; although recent investigations have tended to report a correlation. Indeed, the early documents observed little evidence for a relation between cognitive impairment and depression. However, some recent investigations suggest that cognitive disorders are exacerbated in the moderate to severe range of depression.

Limitations

Our study limitation was lack of previous studies in the research area in evaluated field, including mood disorders related to the multiple sclerosis; thus, we have reached a review study through searching the studies in wider time.

Acknowledgement

The study is part of a master's degree thesis in Shahid Beheshti University of Medical Science

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

All relevant ethical standards were observed in all stages of implementation.

Funding

None

References

1. Arnett PA, Barwick FH, Beeney JE. Depression in multiple sclerosis: review and theoretical proposal. Journal of the International Neuropsychological Society. 2008;14(5):691-724.
2. Feinstein A. Multiple sclerosis and depression. Multiple Sclerosis Journal. 2011;17(11):1276-81.
3. Carta M, Moro MF, Lorefice L, Trincas G, Cocco E, Del Giudice E, et al. The risk of bipolar disorders in multiple sclerosis. Journal of affective disorders. 2014;155:255-60.
4. Womer FY, Wang L, Alpert KI, Smith MJ, Csernansky JG, Barch DM, et al. Basal ganglia and thalamic morphology in schizophrenia and bipolar disorder. Psychiatry Research: Neuroimaging. 2014;223(2):75-83.
5. Moore P, Hirst C, Harding KE, Clarkson H, Pickersgill TP, Robertson NP. Multiple sclerosis relapses and depression. Journal of psychosomatic research. 2012;73(4):272-6.
6. Dalton EJ, Heinrichs RW. Depression in multiple sclerosis: a quantitative review

[Downloaded from mail.intjmi.com on 2026-11-19]

of the evidence. Neuropsychology. 2005;19(2):152.
7. Luo X, Mao Q, Shi J, Wang X, Li C-SR. Putamen gray matter volumes in neuropsychiatric and neurodegenerative disorders. World journal of psychiatry and mental health research. 2019;3(1).
8. Schubert DS, Foliart RH. Increased depression in multiple sclerosis patients: A meta-analysis. Psychosomatics: Journal of Consultation and Liaison Psychiatry. 1993.
9. Wallin MT, Wilken JA, Turner AP, Williams RM, Kane R. Depression and multiple sclerosis: Review of a lethal combination. Journal of Rehabilitation Research & Development. 2006;43(1).
10. Mohr DC, Hart SL, Goldberg A. Effects of treatment for depression on fatigue in multiple sclerosis. Psychosomatic medicine. 2003;65(4):542-7.
11. Ziemssen T. Multiple sclerosis beyond EDSS: depression and fatigue. Journal of the neurological sciences. 2009;277:S37-S41.
12. Gay MC, Vrignaud P, Garitte C, Meunier C. Predictors of depression in multiple sclerosis patients. Acta Neurologica Scandinavica. 2010;121(3):161-70.
13. Arnett P, Randolph J. Longitudinal course of depression symptoms in multiple sclerosis. Journal of Neurology, Neurosurgery & Psychiatry. 2006;77(5):606-10.
14. Patten SB, Metz LM. Depression in multiple sclerosis. Psychotherapy and Psychosomatics. 1997;66(6):286-92.
15. Janardhan V, Bakshi R. Quality of life in patients with multiple sclerosis: the impact of fatigue and depression. Journal of the neurological sciences. 2002;205(1):51-8.
16. Fruewald S, Loeffler-Stastka H, Eher R, Saletu B, Baumhacki U. Depression and quality of life in multiple sclerosis. Acta Neurologica Scandinavica. 2001;104(5):257-61.
17. Bakshi R, Shaikh Z, Miletich R, Czarnecki D, Dmochowski J, Henschel K, et al. Fatigue in multiple sclerosis and its relationship to depression and neurologic disability. Multiple Sclerosis Journal. 2000;6(3):181-5.
18. Beiske A, Svensson E, Sandanger I, Czujko B, Pedersen E, Aarseth J, et al. Depression and anxiety amongst multiple sclerosis patients. European journal of neurology. 2008;15(3):239-45.
19. Solaro C, Gamberini G, Masuccio FG. Depression in multiple sclerosis: epidemiology, aetiology, diagnosis and treatment. CNS drugs. 2018;32(2):117-33.
20. Patten SB, Marrie RA, Carta MG. Depression in multiple sclerosis. International Review of Psychiatry. 2017;29(5):463-72.
21. Sigitova E, Fišar Z, Hroudová J, Cikánková T, Raboch J. Biological hypotheses and biomarkers of bipolar disorder. Psychiatry and clinical neurosciences. 2017;71(2):77-103.
22. Andrews G, Henderson S, Hall W. Prevalence, comorbidity, disability and service utilisation: overview of the Australian National Mental Health Survey. The British Journal of Psychiatry. 2001;178(2):145-53.
23. Schiffer RB, Wineman NM. Antidepressant pharmacotherapy of depression associated with multiple sclerosis. The American journal of psychiatry. 1990.
24. Minden SL, Orav J, Reich P. Depression in multiple sclerosis. General hospital psychiatry. 1987;9(6):426-34.
25. Joffe RT, Lippert GP, Gray TA, Sawa G, Horvath Z. Mood disorder and multiple sclerosis. Archives of Neurology. 1987;44(4):376-8.

[Downloaded from mail.intjmi.com on 2026-11-19]

26. Sadovnick A, Remick R, Allen J, Swartz E, Yee I, Eisen K, et al. Depression and multiple sclerosis. Neurology. 1996;46(3):628-32.
27. Chwastiak L, Ehde DM, Gibbons LE, Sullivan M, Bowen JD, Kraft GH. Depressive symptoms and severity of illness in multiple sclerosis: epidemiologic study of a large community sample. American journal of Psychiatry. 2002;159(11):1862-8.
28. Eshaghi A, Prados F, Brownlee WJ, Altmann DR, Tur C, Cardoso MJ, et al. Deep gray matter volume loss drives disability worsening in multiple sclerosis. Annals of neurology. 2018;83(2):210-22.
29. Feinstein A. An examination of suicidal intent in patients with multiple sclerosis. Neurology. 2002;59(5):674-8.
30. Shelton RC, Hollon SD, Purdon SE, Loosen PT. Biological and psychological aspects of depression. Behavior Therapy. 1991;22(2):201-28.
31. Rabins PV, Brooks BR, O'donnell P, Pearlson GD, Moberg P, Jubelt B, et al. Structural brain correlates of emotional disorder in multiple sclerosis. Brain. 1986;109(4):585-97.
32. Honer WG, Hurwitz T, Li DK, Palmer M, Paty DW. Temporal lobe involvement in multiple sclerosis patients with psychiatric disorders. Archives of Neurology. 1987;44(2):187-90.
33. Ron M, Logsdail S. Psychiatric morbidity in multiple sclerosis: a clinical and MRI study. Psychological medicine. 1989;19(4):887-95.
34. Pujol J, Bello J, Deus J, Marti-Vilalta J, Capdevila A. Lesions in the left arcuate fasciculus region and depressive symptoms in multiple sclerosis. Neurology. 1997;49(4):1105-10.
35. Zorzon M, de Masi R, Nasuelli D, Ukmar M, Pozzi Mucelli R, Cazzato G, et al. Depression and anxiety in multiple sclerosis. A clinical and MRI study in 95 subjects. Journal of neurology. 2001;248(5):416-21.
36. Cotter J, Granger K, Backx R, Hobbs M, Looi CY, Barnett JH. Social cognitive dysfunction as a clinical marker: A systematic review of meta-analyses across 30 clinical conditions. Neuroscience & Biobehavioral Reviews. 2018;84:92-9.
37. Skvarc DR, Berk M, Byrne LK, Dean OM, Dodd S, Lewis M, et al. Post-operative cognitive dysfunction: an exploration of the inflammatory hypothesis and novel therapies. Neuroscience & Biobehavioral Reviews. 2018;84:116-33.
38. Silveira C, Guedes R, Maia D, Curral R, Coelho R. Neuropsychiatric symptoms of multiple sclerosis: state of the art. Psychiatry investigation. 2019;16(12):877.
39. Jiang C, Zhou H, Chen L, Zhou Z. Problem Solving Therapy Improves Effortful Cognition in Major Depression. Frontiers in Psychiatry. 2021;12.
40. Arnett PA, Higginson CI, Randolph JJ. Depression in multiple sclerosis: relationship to planning ability. Journal of the International Neuropsychological Society. 2001;7(6):665-74.
41. Landrø NI, Celius EG, Sletvold H. Depressive symptoms account for deficient information processing speed but not for impaired working memory in early phase multiple sclerosis (MS). Journal of the neurological sciences. 2004;217(2):211-6.
42. Bol Y, Duits AA, Hupperts RM, Verlinden I, Verhey FR. The impact of fatigue on cognitive functioning in patients with multiple sclerosis. Clinical rehabilitation. 2010;24(9):854-62.
43. Panza F, D'Introno A, Colacicco AM, Capurso C, Del Parigi A, Caselli RJ, et al. Depressive symptoms, vascular risk factors and mild cognitive impairment. Dementia and geriatric cognitive disorders. 2008;25(4):336-46.

[Downloaded from mail.intjmi.com on 2026-11-19]

44. Petersen JZ, Porter RJ, Miskowiak KW. Clinical characteristics associated with the discrepancy between subjective and objective cognitive impairment in depression. Journal of Affective Disorders. 2019;246:763-74.
45. Nicholl CR, Lincoln NB, Francis VM, Stephan TF. Assessment of emotional problems in people with multiple sclerosis. Clinical rehabilitation. 2001;15(6):657-68.
46. Smith S, Young C. The role of affect on the perception of disability in multiple sclerosis. Clinical rehabilitation. 2000;14(1):50-4.
47. Krupp LB, Alvarez LA, LaRocca NG, Scheinberg LC. Fatigue in multiple sclerosis. Archives of neurology. 1988;45(4):435-7.
48. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Archives of neurology. 1989;46(10):1121-3.
49. Vercoulen JH, Hommes OR, Swanink CM, Jongen PJ, Fennis JF, Galama JM, et al. The measurement of fatigue in patients with multiple sclerosis: a multidimensional comparison with patients with chronic fatigue syndrome and healthy subjects. Archives of neurology. 1996;53(7):642-9.
50. Schwartz CE, Coulthard-Morris L, Zeng Q. Psychosocial correlates of fatigue in multiple sclerosis. Archives of physical medicine and rehabilitation. 1996;77(2):165-70.
51. Ford H, Trigwell P, Johnson M. The nature of fatigue in multiple sclerosis. Journal of psychosomatic research. 1998;45(1):33-8.
52. Schreurs KM, de Ridder DT, Bensing JM. Fatigue in multiple sclerosis: reciprocal relationships with physical disabilities and depression. Journal of psychosomatic research. 2002;53(3):775-81.
53. Hickie IB, Hooker AW, Bennett BK, Hadzi-Pavlovic D, Wilson AJ, Lloyd AR. Fatigue in selected primary care settings: sociodemographic and psychiatric correlates. Medical Journal of Australia. 1996;164(10):585-8.
54. Feinstein A. The neuropsychiatry of multiple sclerosis. The Canadian Journal of Psychiatry. 2004;49(3):157-63.
55. Mohr DC, Boudewyn AC, Goodkin DE, Bostrom A, Epstein L. Comparative outcomes for individual cognitive-behavior therapy, supportive-expressive group psychotherapy, and sertraline for the treatment of depression in multiple sclerosis. Journal of consulting and clinical psychology. 2001;69(6):942.
56. Siegert RJ, Abernethy D. Depression in multiple sclerosis: a review. Journal of Neurology, Neurosurgery & Psychiatry. 2005;76(4):469-75.
57. Feinstein A, Magalhaes S, Richard J-F, Audet B, Moore C. The link between multiple sclerosis and depression. Nature Reviews Neurology. 2014;10(9):507-17.
58. Charil A, Filippi M. Inflammatory demyelination and neurodegeneration in early multiple sclerosis. Journal of the neurological sciences. 2007;259(1-2):7-15.
59. Husain MM, McDonald WM, Doraiswamy PM, Figiel GS, Na C, Escalona PR, et al. A magnetic resonance imaging study of putamen nuclei in major depression. Psychiatry Research: Neuroimaging. 1991;40(2):95-9.
60. Hallahan B, Newell J, Soares JC, Brambilla P, Strakowski SM, Fleck DE, et al. Structural magnetic resonance imaging in bipolar disorder: an international collaborative mega-analysis of individual adult patient data. Biological psychiatry. 2011;69(4):326-35.
61. Hibar D, Westlye LT, van Erp TG, Rasmussen J, Leonardo CD, Faskowitz J, et al. Subcortical volumetric abnormalities in

[Downloaded from mail.intjmi.com on 2026-11-19]

bipolar disorder. Molecular psychiatry. 2016;21(12):1710-6.
62. Rimol LM, Hartberg CB, Nesvåg R, Fennema-Notestine C, Hagler Jr DJ, Pung CJ, et al. Cortical thickness and subcortical volumes in schizophrenia and bipolar disorder. Biological psychiatry. 2010;68(1):41-50.
63. Haber SN, Calzavara R. The cortico-basal ganglia integrative network: the role of the thalamus. Brain research bulletin. 2009;78(2-3):69-74.
64. Floresco SB. The nucleus accumbens: an interface between cognition, emotion, and action. Annual review of psychology. 2015;66:25-52.
65. Patten SB, Metz LM, Reimer MA. Biopsychosocial correlates of lifetime major depression in a multiple sclerosis population. Multiple Sclerosis Journal. 2000;6(2):115-20.
66. Diagnostic APA. Statistical Manual of mental disorders. Washington, DC: American Psychiatric Association; 1994.
67. Kenealy PM, Beaumont GJ, Lintern T, Murrell R. Autobiographical memory, depression and quality of life in multiple sclerosis. Journal of clinical and experimental neuropsychology. 2000;22(1):125-31.
68.Feinstein A, O'Connor P, Feinstein K. Multiple sclerosis, interferon beta-1b and depression. Journal of neurology. 2002;249(7):815-20.
69.Ackerman K, Rabin B, Heyman R, Frank E, Anderson B, Baum A, editors. Stressful life events precede multiple sclerosis disease exacerbations. Psychosomatic Medicine; 2000: LIPPINCOTT WILLIAMS & WILKINS 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.
70.Dalos NP, Rabins PV, Brooks BR, O'Donnell P. Disease activity and emotional state in multiple sclerosis. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1983;13(5):573-7.
71.Franklin GM, Nelson LM, Heaton RK, Burks JS, Thompson DS. Stress and its relationship to acute exacerbations in multiple sclerosis. Journal of Neurologic Rehabilitation. 1988;2(1):7-11.
72.Mohr DC, Goodkin D, Bacchetti P, Boudewyn A, Huang L, Marrietta P, et al. Psychological stress and the subsequent appearance of new brain MRI lesions in MS. Neurology. 2000;55(1):55-61.
73.Group GC. The Goldman Consensus statement on depression in multiple sclerosis. Multiple Sclerosis Journal. 2005;11(3):328-37.
74.Farshidfar Z , Faeghi F,Hagighatkhah HR,Abdolmohammadi J, et al . The optimization of MRI pulse sequence in order to better detection of MS plaques in cognitive dysfucnctions.J Biomed Phys Eng.2017 sep1;7(3):265-270.PMID 29082217;PMCID:PMC5654132
75.Ashrafi F,Behnam B,Arabahmadi M,Sanei Thheri M,Haghighatkhah HR , et al.correlation of MRI findings and cognitive functions in MS patients using Montreal cognitive assessment test.Med J Islam Repub Iran.2016 Apr 17;30:357.PMD: 27453887;PMCID:PMC4934419

[Downloaded from mail.intjmi.com on 2026-11-19]