

PSYCHOTHERAPY

Unmet psychosocial needs of people with multiple sclerosis

Jan PRASKO¹, Jakub VANEK¹, Marie OCISKOVA¹, Kamila BELOHRADOVA¹,
Michaela HOLUBOVA^{1,4,5}, Krystof KANTOR¹, Milos SLEPECKY³, Tomas SOLLAR³

¹Department of Psychiatry, Faculty of Medicine and Dentistry, University Palacky Olomouc, University Hospital, 77520 Olomouc, Czech Republic, ²Institute for Postgraduate Education in Health Care, Prague, Czech Republic, ³Department of Psychology Sciences, Faculty of Social Science and Health Care, Constantine the Philosopher University in Nitra, Slovak Republic, ⁴Department of Psychiatry, Hospital Liberec, Czech Republic, ⁵Department of Pedagogy and Psychology, Faculty of Science, Humanities and education, Technical University of Liberec, Czech Republic.

Correspondence to: prof. Jan Prasko, MD, PhD, Department of Psychiatry, Faculty of Medicine and Dentistry, Palacky University Olomouc, University Hospital, I. P. Pavlova 6, 77520 Olomouc, Czech Republic
TEL: +420 603 414 930; E-MAIL: praskojan@seznam.cz

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Abstract

BACKGROUND: Multiple sclerosis (MS) is an autoimmune illness in the immune system that attacks myelin segments in the brain and spinal cord. Symptoms are diverse and unpredictable, appearing in varying combinations and patterns. Many patients suffer from additional behavioural and psychiatric symptoms, ranging from stress-related disorders, neurotic and affective disorders to psychotic disorders and even cognitive impairment and dementia. This review aimed at identifying unmet needs accompanying MS (that can be combined with unmet needs in psychiatric disorders).

METHOD: Articles published between January 1970 and December 2021 were screened by a computerized search of the literature, using keywords multiple sclerosis, in successive combination with needs, psychosocial aspects, quality of life, psychiatric diseases, adjustment disorder, depression, cognitive deficit, anxiety disorder, psychopharmacs, psychotherapy, or cognitive behavioural therapy, and family.

RESULTS: There is a significant, though not a very strong association between stress and exacerbation of MS. Patients with MS have various psychosocial needs. However, fulfilling them may be challenging. Problematic areas include lifestyle and self-care, work and social environment and even sexual relationships. The individual's reaction to the MS diagnosis considerably depends on their personality traits and coping capacities. Unexpected exacerbations may arise and interfere with the patient's desires and plans. Psychological and emotional challenges associated with MS can reflect the immediate effects of the disease, such as structural brain abnormalities and disease characteristics, and the secondary implications of the complex interplay of long-standing personality dynamics with the adaptive demands of dealing with compromised functioning and uncertainty. MS associated with the psychiatric condition can pose a challenge for effective treatment. Sometimes it might be difficult to distinguish whether the symptoms are caused by MS, psychiatric disorder, unmet psychosocial needs or an adverse effect of the treatment.

CONCLUSION: A neuropsychologically informed psychotherapy could be an essential component of our patients' treatment regimens as they cope with the losses in adaptive functioning, inefficiencies in cognitive processing, and the compromising effects of stress and fatigue on neuropsychological status and quality of life.

INTRODUCTION

Multiple sclerosis (MS) is an autoimmune illness that manifests by the immune system attacking myelin segments in the brain and spinal cord (Kamber *et al.* 1995; McDonald 2000; Dymment & Ebers 2002; Lassmann *et al.* 2007). The scar tissue that replaces affected areas of myelin segments interferes with the transmission of nerve impulses, causing neurobehavioral deficits (Lincoln *et al.* 2020a;b). The disease usually starts in early or mid-adulthood and is characterized by repeated episodes that occur irregularly over many years. Each episode brings new clinical symptoms (Lassmann *et al.* 2007). The symptoms and the extent of disability experienced with MS vary, depending on the location and scale of the myelin destruction (Kamber *et al.* 1995).

Consequently, there is high interindividual variability in both symptoms and progress of the disorder (Rao 1986; McDonald 2000; Dymment *et al.* 2002). Lesions are located dispersedly in CNS, brainstem, and spinal cord and may cause focal or complex symptoms. These range from weakness, pain, intermittent dizziness, chronic imbalance and gait disturbance to sensory impairment, motor disturbances, internuclear ophthalmoplegia, or trigeminal neuralgia (Kamber *et al.* 1995; Pula *et al.* 2013). The impairment may eventually result in physical disability and even confine the patient to bed.

The aetiology of the autoimmune reaction against the body's myelin is unknown, with research models pointing toward an interplay between genetic and environmental factors, including exposure to Epstein-Barr virus or geographic factors, like the amount of sunlight exposure (Milo & Kahana 2010). Since the concordance rate for monozygotic twins is only about 30%, environmental factors play a significant role (Noseworthy *et al.* 2000). MS is most prevalent in north Europe, somewhat less prevalent in North America and rare in Japan and tropical countries (Dymment *et al.* 2002). In countries where it is prevalent, its incidence of 50 per 100,000 makes it one of the most common nervous system diseases (Rosati 2001; Goodin *et al.* 2016; Wallin *et al.* 2019; Goodin *et al.* 2021). MS has a female-to-male ratio of about 3 to 2, and its progress is often more rapid in females than in males. About 70 % developed their first symptoms between ages 21 and 40 (Wallin *et al.* 2019; Iljicsov *et al.* 2021).

MS is classified into several subtypes (Lublin & Reingold 1996). Most patients with initial diagnosis (85 %) have a relapsing-remitting form, characterized by periods of neurologic symptoms followed by remissions

(Frohman 2003). For many, the disorder progresses into a secondary progressive form with or without irregular relapses or remissions. Primary progressive MS is defined as disease progression from the onset with infrequent plateaus and temporary minor improvements (Lublin & Reingold 1996; Pilutti *et al.* 2019). This subtype represents about 10 % of MS patients (Frohman 2003). A least common progressive relapsing subtype is characterized by progressive disease at the onset with periods of disease exacerbation and permanent progression between relapses (Lublin & Reingold 1996; Pilutti *et al.* 2019).

The link between MS and its neuropsychiatric expressions has been well recognized. Psychiatric patients show a higher prevalence of MS (Lyoo *et al.* 1996). For instance, MS was newly diagnosed in 0.8 % of individuals with mental disorders, a rate that is approximately 13 times higher than the prevalence of MS in the general population (Lyoo *et al.* 1996; Lincoln *et al.* 2020b).

Our paper aims to identify the psychosocial needs of people with multiple sclerosis (MS), map out psychiatric comorbidities, and identify whether they can be addressed through psychiatric care, psychoeducation, psychotherapy, counselling, or social work.

METHOD

PubMed and Web of Science databases were searched for articles published between January 1970 and December 2021 using the following terms: „multiple sclerosis“, in successive combination with „needs“, „psychosocial aspects“, „quality of life“, „psychiatric diseases“, „adjustment disorder“, „depression“, „cognitive deficit“, „anxiety disorder“, „psychopharmac“, „psychotherapy“, or „cognitive behavioural therapy“, and „family“. The included works had to be (1) published in peer-reviewed journals; (2) prospective or retrospective original studies in humans; or (3) reviews on a relevant topic; and (4) with adult subjects. Excluded were (1) conference abstracts; (2) commentaries and dissertations (3) subjects younger than 18 years old. A flow diagram (Fig. 1) describes the selection process and summarizes the total number of screened papers and those included in the review process.

RESULTS

Patients with MS have various psychosocial needs. Many of them also suffer from behavioural and psychiatric symptoms, including emotional lability, adjustment disorders, depression, euphoria, mania, anxiety disorders, insomnia, sexual dysfunction, psychosis, suicidality, personality changes, cognitive impairment, and dementia (Yang & Wichser 2020). Neurologists, mental health professionals, and patients' families address many psychosocial needs accompanying conditions. However, some of them may remain unmet.

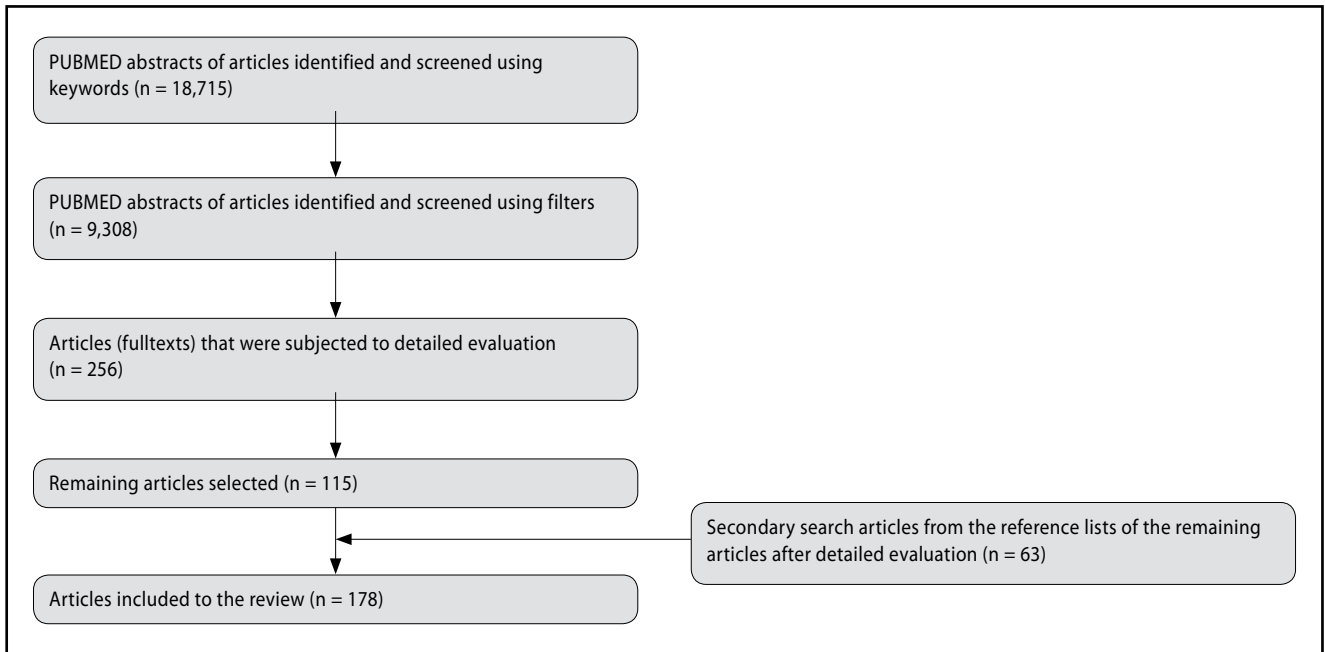


Fig. 1. Summary of the selection process

Keywords: (multiple sclerosis and needs) OR (multiple sclerosis and psychosocial aspects) OR (multiple sclerosis and quality of life) OR (multiple sclerosis and psychiatric diseases) OR (multiple sclerosis and adjustment disorder) OR (multiple sclerosis and depression) OR (multiple sclerosis and cognitive deficit) OR (multiple sclerosis and anxiety disorder) OR (multiple sclerosis and psychopharmacs) OR (multiple sclerosis and psychotherapy) OR (multiple sclerosis and psychoeducation) OR (multiple sclerosis and cognitive behavioural therapy) OR (multiple sclerosis and family)

Filters activated: Comparative Study, Consensus Development Conference, Clinical Trial, Phase IV, Abstract, Humans, English, Adult: 19+ years

Psychological distress and MS activity

The onset of MS correlates with reduced immune system functioning following severe life stressors (Cohen *et al.* 1991; Lincoln *et al.* 2020a). Many patients with MS have observed a connection between psychosocial distress and increased disease activity (Mohr *et al.* 2002). One study found that psychological conflict and disruption in daily routine are weakly associated with new gadolinium-enhancing MRI lesions but not with clinical exacerbations (Mohr *et al.* 2000). Reducing distress or depression associated with MS improves the quality of life and positively affects the underlying pathophysiology of the disease (Mohr *et al.* 2001; Hasanpour Dehkordi 2016). Research has also suggested that effective coping can moderate the relationship between stress and MS disease activity (Mohr *et al.* 2002; Lincoln *et al.* 2020b).

The Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology concluded that even though a relationship between psychosocial stress and the onset or an exacerbation of MS is possible, the best medical evidence failed to establish a causal relationship (American Academy of Neurology and the MS Council for Clinical Practice Guidelines 2002). However, several subsequent studies confronted this conclusion. A self-reported series of stressful events increased the risk of relapse twofold during the following four weeks (Buljevac *et al.* 2003). A meta-analysis of published reports found

a significant but modest association between stress and exacerbation of MS (Mohr *et al.* 2004; Schirmer 2019). A nationwide cohort study in Denmark (Li *et al.* 2004) reported a higher MS risk in parents who lost a child than in parents who did not experience this trauma, suggesting that the psychological distress induced by the death of a child may play a role.

Distress connected with the disease itself

As with other chronic illnesses, the individual's reaction to the MS diagnosis considerably depends on the individuals' personality traits (Dymecka & Bidzan 2018). Patients with recent diagnoses can struggle to accept the diagnosis and continue to search for an alternative explanation of their problems. In other cases, patients may feel a sense of relief at finally being given a diagnosis to validate what they have been experiencing (Cardamone *et al.* 2018). Other patients may respond with panic, mistrust, helplessness, and increased anxiety (Maxeiner *et al.* 2014).

As the diagnosis is accepted, patients may try to assume some control over the disease. Some patients experience abrupt changes in the MS activity, and others observe a more fluctuating course. The long-term experience of living with MS through adulthood requires initial acceptance of the condition and continuing psychological flexibility as the disease changes (Ben-Zacharia & Lublin 2001; Tomas-Roig & Havemann-Reinecke 2019).

Lifestyle needs and issues

The effects of neurological disorders on an individual's lifestyle are varied and complex. Activities of daily living are often altered, and help from family members may be necessary (Arnett *et al.* 2001). The related loss of privacy for most intimate details of everyday life, such as bathing or dressing, may be a part of the general condition. Even when individuals can manage their self-care, the additional time required to carry out most activities may be considered a liability (Beatty & Monson 1996; Arnett *et al.* 1997). When fatigue exacerbates the symptoms of a neurological disorder, as in MS, it may be needed to space out activities or arrange for rest numerous times in the day (Hasanpour Dehkordi 2016; Pilutti *et al.* 2019).

If wheelchairs are used, the environment must be made navigable. Wheelchairs can offer more independence of movement for those with paralysis, those who have difficulty walking because of problems with coordination, or individuals who exhaust quickly and use a wheelchair to keep energy (Dymecka & Bidzan 2018). Persons with NS can usually drive, even with some level of paralysis, if the vehicle is equipped with customized controls. However, driving may not be possible if the disability includes cognitive or perceptual deficits. The disability itself and the expenses related to medical care, rehabilitation, assistance, and other necessities can disturb the patient's financial situation and, therefore, influence a lifestyle that must be adjusted to it (Dymecka & Bidzan 2018).

Vocational needs and issues in MS

Many individuals with MS experience unemployment and underemployment (Bishop *et al.* 2000; Dymecka & Bidzan 2018). Educational attainment, symptom severity, and the presence of cognitive limitations appear to be significant predictors of employment status for some individuals (Roessler *et al.* 2004). Since MS varies widely among persons, each vocational potential must be considered separately. Those with mild symptoms, slowly progressive MS or prolonged periods of remission can be productively employed for many years.

Mobility, communication, vision, affective and cognitive function are common areas that need assessment. Those with communication difficulties, such as slurred speech, may require other types of accommodations or considerations regarding job placement. Those with balance problems may need to avoid circumstances in which falling could be dangerous or need a walking aid, such as a cane or crutch, that could be useful in preventing a fall. If vision is affected, detailed adjustments connected to visual needs may be necessary. Individuals may also benefit from cognitive retraining or memory enhancement programs (Roessler *et al.* 2001; Lincoln *et al.* 2020).

Emotional stress and physical stress can cause a temporary worsening of the symptoms—the degree of emotional and physical stress that the individual

experiences at their job should be considered. Although individuals do not need to curtail physical activity, they should avoid exhausting themselves (Hasanpour Dehkordi 2016; Grazioli *et al.* 2019; Tollár *et al.* 2020; Lincoln *et al.* 2020).

Individuals should also learn to moderate their activities and find levels conducive to optimizing energy. It may be essential to break tasks into smaller steps, resting at intervals between (Halabchi *et al.* 2017; Edwards *et al.* 2017; Edwards *et al.* 2018). Adjusting work hours to specific needs, involving persons in more deskbound work, or using energy-saving tools may be suitable to grow work capability (Ziliotto *et al.* 2020). Because heat also affects symptoms, individuals should avoid hot and humid environments. They should avoid extended contact with the sun and stay in an air-conditioned setting as much as possible on hot days.

Although there are limitations related to the illness, many people with MS can continue to work with only minor adjustments (Lincoln *et al.* 2020). Loss of time at work during exacerbations should be expected; however, generally, these episodes are not excessive. Assistive devices, new equipment, accessible restrooms, and timetable adjusting can enhance the individual's ability to continue work.

Social needs and issues

Many factors associated with MS affect social functioning (Hegedüs *et al.* 2015). A supportive environment, including the family circle, plays an instrumental role in individuals' response to disability (Dymecka & Bidzan 2018; Wilski *et al.* 2021). However, misinterpretation or misperception of the individuals' disability and associated functional limitations can prevent effective social interaction and personal adjustment (Wilski *et al.* 2019). The consequences of MS, which may involve emotional instability or cognitive problems, may be perceived by others as rudeness, insensitivity, or irresponsibility rather than manifestations of the condition itself (Tan-Kristanto & Kiropoulos 2015; das Nair *et al.* 2016; Taylor *et al.* 2021). The misunderstanding may cause people to avoid communication difficulties because they avoid understanding what they are saying.

As a chronic illness with a disability, MS affects family members and social interactions. Members of the family may become overly protective, shielding individuals from responsibility. Individuals may be excluded from family problems or decision making. In other instances, family members may find it difficult to express anger toward their family member with a disability. On the other hand, the patients themselves can be troubled with the idea of becoming a burden to their family or friends. This can result in social withdrawal, negatively affecting their close relationships (Tan-Kristanto & Kiropoulos 2015; Wilski *et al.* 2021).

Wheelchair use may also affect social function. Because not all social events or situations are accessible to individuals using a wheelchair, they may either avoid

an activity or make special arrangements to attend it. Although most public places have provided accessibility, some are more desirable than others. Also, different angles of eye contact can create multiple emotional impacts for individuals in wheelchairs, who must continually look upward at their peers (Jones & Amtmann 2015; Gay *et al.* 2017).

Social interaction difficulties associated with MS may manifest in poor social performance, social anxiety, and low self-esteem. Individuals with such a disorder may experience considerable frustration in the fight to cope with social demands (Gay *et al.* 2017; Fisher *et al.* 2020). In some patients, neurological conditions result in impaired capacity for social perceptiveness, distractibility, an absence of social initiation, or behavioural problems (e.g., disinhibition or impulsivity) (Fisher *et al.* 2020). These symptoms can significantly affect individuals' interaction ability in social settings (Heffer-Rahn & Fisher 2018). In these instances, social skills training or continuing supervision or prompting in the social setting can help patients integrate more fully into social situations.

Psychological and emotional challenges

It is often difficult to determine the degree to which behavioural and affective changes originate from MS itself and the degree to which they are psychologically induced. Most patients with MS are young persons who have lived through formative years of adolescence as relatively healthy persons and are at an age in which they are beginning to adopt many social and financial responsibilities, such as choosing a career, establishing intimate personal relationships, and perhaps starting a family (Goodkin *et al.* 1991). When the diagnosis of MS is confirmed, the limitations and unpredictability of the condition can harshly disturb the person's self-concept. Limitations in physical abilities, activities and social relationships call for significant initial psychosocial adjustment, alteration of self-concept, and continual readjustment as exacerbations, remissions, and new disabling features of the condition occur. Eklund & MacDonald (1991) found that those struggling with this neurological condition expressed the need for help in two primary areas: (a) accepting the reality of the disease and (b) learning how to lead the best possible life with it.

Adjustment problems

The necessity of learning compensatory strategies for some activities and social interactions makes the psychological adjustment to MS complex and demanding. Available treatment options are limited and directed mainly toward controlling symptoms or preventing complications (Malekzadeh *et al.* 2019). Consequently, patients with MS may feel they have little control over the condition or future. The rate of progression and degree of loss of functional capacity in many patients with MS are often unpredictable. When the

illness progressively debilitates, as is typical for many patients with MS, individuals must continually readapt as additional functional capacity is lost. Under these conditions, they may experience a helpless rage or resentment because of an illness they have no control over (Mohr *et al.* 2000). The uncertainty about whether disability will be minimal or progress to severe disability can produce hardship. On some occasions, the seek for retribution becomes an opposing force, corroding the person's life as they continually seek justice. However, most individuals with neurological disorders adjust and learn to be self-reliant, although their ability to care for their basic physical needs decreases over time (Mohr *et al.* 2000).

Many patients' symptoms require support in care and function by their very nature. Those who experience paralysis may feel an increased sense of vulnerability, fearing that escaping from a dangerous situation or defending themselves against a threat would be difficult or impossible. Persons may harbor bitterness over the dependency imposed by the illness. Their reaction may vary from overdependence to overcompensation, in which they take unnecessary risks to test or prove their independence and strength (Gay *et al.* 2017; Heffer-Rahn & Fisher 2018).

Impairment of bladder and bowel control may be a challenging area of adjustment. When patients lose the capacity to care for basic physical needs, they may struggle to accept it. Learning to accept necessary assistance from others for basic needs, such as feeding, bowel and bladder care, personal hygiene, requires reconstituting self-confidence and attitudes towards privacy (Fruehwald *et al.* 2001; Gay *et al.* 2017; Heffer-Rahn & Fisher 2018). Not only are such activities private and catastrophes a potential source of embarrassment, but both may also trigger memories of shame and humiliation experienced in early childhood when control of these most basic bodily functions was a central point of development.

Other individuals use their experience to create public awareness of persons with a disability and educate others about disability problems (Vostrý *et al.* 2020; Lincoln *et al.* 2020b). Just as neurological conditions have a spectrum of functional consequences, the adjustment of individuals with neurological conditions is highly individualized, and no two people with the same disability will react the same.

PSYCHIATRIC DISORDERS IN MS PATIENTS

Depression

Depression has been considered the most common mental state change associated with MS. Feinstein (1999) found that 80 of 100 consecutive referrals with MS to a neuropsychiatric clinic had mood disorders, with the majority being major depression. The lifetime prevalence of depression in MS ranges from 25%–50% (Feinstein *et al.* 2004). The causes for depression are

multifactorial and can reflect structural brain abnormalities (Feinstein *et al.* 2004), disease exacerbations and course (Feinstein 1999), and secondary psychosocial adaptive challenges. Fatigue and physical disability can contribute to depressed mood, and depression also may be mediated by the inability to participate in recreational activities (Voss *et al.* 2002).

The severity of illness, including the degree of pain and the functional loss, has been more closely linked with depression than the duration of the disease. Compared with patients with the primary progressive course, those with the relapsing course have 2.6-fold more lifetime comorbidity of major depression (Zabad *et al.* 2005). Their increased susceptibility to depression may be attributed to an earlier onset of MS symptoms and being subjected to unanticipated, randomly timed attacks.

Depression is less common when the spinal cord is affected predominantly or exclusively (Chwastiak 2002). Other factors positively associated with depression include younger age, less education, lack of social support, high-stress levels, family history of depression, and a more recent diagnosis of MS. Women with MS are at a higher risk of depression than men (Caine and Schwid, 2002). Depression is also associated with MRI findings of the total lesion (plaque) burden and cerebral atrophy (Bakshi *et al.* 2000), right frontal lobe lesion load and right temporal brain volume loss (Zorzon *et al.* 2001). However, many of these MRI abnormalities are nonspecific.

There has been much debate about the direction of causality in the attempts to understand the relationship between physical disease and mood disorders (Hegedüs *et al.* 2015). In particular, there has been speculation that certain illnesses like MS may cause depression via direct biological mechanisms. Although euphoria is classically described as a feature of late-stage MS, associated with marked demyelination in prefrontal areas, depression is a more frequently encountered mood change (Zorzon *et al.* 2001; David 2007). Frontal cognitive impairment is significantly related to depression symptoms, suggesting the involvement of shared anatomical circuits (Filippi *et al.* 1994). Studies of plaque loci in MS also have suggested an association of depression with lesions in the temporal lobe, but these reports have not shown lateralized effects (Goodstein & Ferrel 1977; Mathews 1979; Honer *et al.* 1987). Depression among individuals with MS correlates more strongly with the degree of HPA axis dysfunction than with the level of neurological impairment (Fassbender *et al.* 1998; Gold & Irwin 2006; Kale *et al.* 2010), consistent with the theory that HPA axis dysfunction contributes to major depressive disorder in general (Plotsky *et al.* 1998).

Whatever the cause of patients' MS-associated depression, depressive symptoms are likely to impair MS patients' ability to adhere to treatment regimens, which can be arduous (Hegedüs *et al.* 2015; Dymecka

& Bidzan 2018). Research has suggested that cognitive dysfunction is an essential factor in determining the quality of life of people with MS, and cognitively impaired patients are more likely to be unemployed, divorced, and depressed (Brassington & Marsh 1998; Webster *et al.* 2017). Depression can also impact cognitive functioning in patients with MS (Arnett *et al.* 2001; Hegedüs *et al.* 2015).

Emotional dysregulation/dyscontrol

Emotional dysregulation in MS may manifest in "pathological laughing and cry" (PLC) that is defined "as sudden, involuntary displays of laughing or crying or both, without subjective feelings of pronounced sadness or euphoria" (Feinstein & Feinstein 2001). The phenomenon was demonstrated in 10% of community-based MS patients (Feinstein *et al.* 1997) and is thought to indicate generalized psychological distress that warrants clinical attention (Feinstein & Feinstein 2001).

La belle indifference

Some leading examples of belle indifference probably involved patients with multiple sclerosis who suffered from difficulties in a movement that were thought to be psychological and had frontal lobe lesions that left them happier than the average patient with paralysis (Pratt 1951, Surridge 1969).

Mania and euphoria

Other individuals, rather than experiencing depression, experience an inappropriate euphoria. As with depression studies, prevalence rates of bipolar disorder in persons with MS are approximately twice that in the general community (Yang & Wichser 2020). Prevalence rates of euphoria tend to increase with advanced MS. As many as 25% of advanced MS patients will develop some signs of euphoric effect, and MS can induce this so-called secondary mania. Euphoria, seen in about 25% of patients with MS, is a positive emotion inappropriate to the situation (Rabins 1990). Euphoria has been associated with bilateral subfrontal demyelination (Minden & Schiffer 1990) and with a higher rate of neurological and cognitive deficits (Rabins 1990).

Anxiety disorders

Anxiety complaints are also common in patients with MS; however, epidemiologic studies of rates of anxiety are scarce because most research has focused on depression and MS. Indeed, some researchers have suggested that in the absence of any data supporting the correlation between anxiety complaints and CNS lesions, anxiety is a response to psychosocial pressures on the patient or the use of steroids (Zorzon *et al.* 2001).

Although less well studied, anxiety can be a frequent addition to depression and add to the morbidity of MS (Feinstein *et al.* 1999). Korostil & Feinstein (2007) studied 140 outpatients with MS and found that 35.7% had at least one lifetime anxiety disorder, and the

most common anxiety disorders in this sample were GAD (18.6%), panic disorder (10%) and OCD (8.6%). Patients with an anxiety disorder were more likely to be women, have a history of depression, report higher social stress, drink to excess, and suicidal ideation. Risk factors include being a woman, limited social support, and a comorbid diagnosis of depression. Clinicians should assess all MS patients for anxiety disorders as they represent a treatable cause of disability in multiple sclerosis.

Generalized anxiety can be described in numerous medical conditions, including MS (Zorzon *et al.* 2001). Individuals with MS may avoid situations because of genuine concerns about being incapacitated (e.g., fainting) or embarrassed. The diagnosis of agoraphobia ought to be given only when the fear or avoidance is more than that usually associated with these medical conditions (APA 2013).

Insomnia

Accumulating evidence also indicates that insomnia is highly prevalent in individuals with MS (Bamer *et al.* 2008).

Sexual dysfunctions

Damage to the central nervous system, the spinal cord, or the peripheral nerves caused by multiple sclerosis may lead to orgasmic difficulties (Sipski 1998). MS has been implicated in ejaculatory dysfunction and female orgasmic dysfunction (Segraves 2010; APA 2013).

Physiologic reactions need an integral nervous system. Sexual intercourse may be more difficult in spasticity conditions (Schairer *et al.* 2014; Mohammadi *et al.* 2020). In some instances, the stimulation and arousal experienced as part of sexual excitement may make the spasms worse. In other cases, special arrangements for positioning or other technical assistance may be necessary for sexual intercourse. Sexuality is more than the physical act of sex. Some form of sexual expression is possible for almost all individuals with a disability. Persons may need to learn new ways of sexual expression to meet their needs, or in other instances, they may need to control sexual expression. Although the shift of sexual function is a severe shock to self-esteem and a sense of attractiveness, persons can express sexual feelings and needs through various alternate means. Those with neurological disorders can develop long-term intimate relationships that include love, respect, and mutually satisfying expression of sexual feelings.

Psychosis

MS may be associated with delusions (Hägemark *et al.* 2016). In prospective population-based studies, persons with a history of any autoimmune disease are at a 45% increased risk of developing schizophrenia (Slight-Webb *et al.* 2016). Delusional parasitosis has been recognized in a relationship with MS (Kumar & Singh 2009).

Psychotic disorder due to another medical condition may be a single transient state or recurrent, cycling with exacerbations and remissions of the underlying medical condition. It is associated with increased rates of suicide (APA 2013). In the context of chronic conditions such as multiple sclerosis, the psychosis may assume a long-term course (APA 2013).

The confounding clinical problem is that high-dose steroid regimens, often used to treat MS exacerbations, may induce delirium, psychosis, or mania (Sirois 2003). Risperidone (DeSilva *et al.* 2002) and typical antipsychotics may abort steroid psychosis, and lithium given prophylactically may prevent its occurrence (Sirois 2003).

Suicidality

There are critical links between suicidal ideation and behaviour and MS (Coughlin & Sher 2013). The risk of suicide is elevated in MS (Sadovnick *et al.* 1991). Furthermore, screening for suicide risk should be a standard component of psychiatric evaluations in MS patients.

Rates of suicide in persons with MS are reported at up to seven times for an age-matched general population (Feinstein 1997; Şen *et al.* 2021). Retrospective studies correlate suicide with male gender and diagnosis of MS before the age of 30 years, and the risk is highest in the first year after diagnosis (Fredrickson *et al.* 2003). Suicidal patients are more likely to have limited psychosocial support; report more significant social stress; and carry a history of depression, anxiety, alcohol abuse, and a family history of mental illness (Feinstein 1997, Feinstein 2002).

Personality changes

Apathy, lack of concern over their disabilities, lack of initiation, impaired insight, irritability, and poor judgment are personality changes observed in as many as 40% of patients with MS (Mahler 1992) and may be related to frontal lobe dysfunction (Mendez 1995).

Cognitive impairment and dementia

While many patients with MS retain their intellectual function, some do experience a decline in their cognitive capacity. Recent data suggest that 45% to 65% of MS patients will experience cognitive impairment (Amato 2001), although a relatively small fraction will suffer significant functional limitations. The correlation between cognitive decline and the course is less clear, but patients with chronic progressive MS are probably at greater risk than those with the relapsing remitting disease. MS affects a variety of cognitive domains. Memory deficits are a hallmark of this illness, and individuals may have no insight into their memory loss. Recent memory, attention, cognitive processing, conceptual/abstract reasoning, and visual-spatial perception are frequent cognitive impairments.

In contrast, immediate and remote memory and language skills are least disrupted (Webster *et al.* 2017; Goyal *et al.* 2019). The causes of cognitive decline are not yet fully understood. As the pathogenesis of MS generally, but not exclusively, involves demyelinating of white matter tracts, the disruption of communication between intact cortical regions presumably causes cognitive deficits. Studies have correlated the overall loss of brain volume (atrophy) and the total lesion burden with MS (Benedict 2004). Interestingly, data also show that approximately 50% of demyelinating lesions occur in the frontal and parietal lobes, regions of the brain closely associated with cognition (Sperling 2001, Patten *et al.* 2005). Specific findings that have been correlated with a decline in cognitive functioning are callosal corpus atrophy on MRI and increased plaque volume (Huber *et al.* 1992b; Swirsky-Sacchetti *et al.* 1992), frontal lobe atrophy (Locatelli *et al.* 2004), and cortical hypoperfusion in the frontal lobes on SPECT (Pozzilli *et al.* 1991). Furthermore, demyelination of frontal-subcortical circuits in MS on MRI leads to a worsened performance in tasks of conceptual reasoning abilities (Wisconsin Card Sorting Test) (Arnett *et al.* 1994).

Executive functions can be affected in people living with MS (Foong *et al.* 1997), and disruptions in this complex system can manifest in problems with organization, planning, and mental flexibility. Deficits may be identified on tests of concept formation (Beatty & Monson 1996), sequencing and planning (Arnett *et al.* 1997), and verbal fluency (Foong *et al.* 1997).

With MS, the efficient functioning of the attention system may be compromised by reduced processing speed. Patients may feel overwhelmed by the information processing demands associated with daily functioning and complain of memory problems. For some patients with MS, what may appear as a deficit in memory retrieval may reflect disruptions in the acquisition stage of learning associated with slowed processing (DeLuca *et al.* 1994).

The pattern of cognitive difficulties in MS patients seems to be distinct from the one that is typical for neurodegenerative disorders like Alzheimer's disease. Some theorists have suggested that this pattern is characteristic of what has been described as subcortical dementias. However, other researchers have cautioned that there may not be any single pattern of cognitive difficulty associated with MS, but various problems manifest in one or more cognitive domains with other functions remaining normal (Ryan *et al.* 1996).

It generally has been reported that cognitive impairment in people with MS seems unrelated to the duration of the condition or neurological disability status (Rao *et al.* 1991). Most studies have not established an association between the degree of cognitive impairment and duration of illness, and cognitive decline can be detected even in the incipient stage of MS (Amato 2001). The length of the condition is not necessarily

related to disease activity, and physical disability status may reflect areas of nervous system involvement that are not related to cognitive functioning. Problems in-memory processing can be seen in 40%–60% of people with MS (Brassington & Marsh 1998).

Memory is a complex neuropsychological system, and some areas are more susceptible to disruption by MS while others remain relatively unaffected. Recent memory (i.e., new learning and retention) has been a significant focus of study, and one aspect of recent memory that has been implicated as being affected by MS is retrieval, that is, the ability to recall information that has been recently learned (Rao *et al.* 1989). The deficit in retrieval may be demonstrated by poor performances on recall measures in contrast to relatively intact abilities in recognition memory. However, researchers also have considered that problems in the beginning stages of learning or acquisition—which also can include aspects of working memory—may be responsible for the difficulties with information recall that can be seen with MS (DeLuca *et al.* 1994). If processing capacity is overwhelmed, patients may not “get” all the information they are trying to remember, and the information they can process may not be encoded efficiently enough into long-term storage to permit recall later. Remote memory also has been investigated in people with MS, but the results here are again equivocal, with some researchers identifying problems (Beatty *et al.* 1989) whereas others have not (Rao *et al.* 1991). Perhaps we ultimately may discover that the memory processing difficulties experienced by people living with MS are heterogeneous, and the overall results of studies—while helpful in advancing our knowledge of the impact of MS on different parts of the memory system—may not fully describe the experience of anyone personally who has the condition (Beatty *et al.* 1996).

MS eventually causes dementia in most cases, and given that this development typically occurs in the setting of a well-established disease, there is little diagnostic difficulty (McIntosh-Michaelis *et al.* 1991).

FULFILLING UNMET NEEDS IN PATIENTS WITH MS

Lifelong treatment of MS requires a multidisciplinary approach that addresses patients' multiple needs and psychiatric comorbidities (Vostrý *et al.* 2020; Ziliotto *et al.* 2020). This includes not only somatic care but a psychosocial approach as well. The authors wanted to introduce some of these methods in this review.

Psychoeducational groups

In many countries, there are psychoeducational support groups for patients with MS. Some groups are conducted in hospital settings and meet daily or several times per week. Outpatient groups meet once per week or every other week. In orientation, psycho-

educational groups provide helpful information for patients experiencing similar problems and an opportunity for group support (e.g., sharing and expressing feelings and concerns and obtaining feedback from group members). Much like classroom instruction, information is provided, followed by group discussion and support (Lincoln *et al.* 2020a). Patients who share the diagnosis meet to learn how to manage problems accompanying sclerosis multiplex; they also share stories and give and receive support from each patient who shares the same diagnosis come together to learn how to handle their illness; they also share stories and give and receive support from each other. Group support not only is helpful for psychological health but has been associated with longevity among patients with sclerosis multiplex (Lincoln *et al.* 2020b). Meetings are held with the patients and their families to educate them about MS. Furthermore, the effect it can have on behaviour and explore the family patterns that are likely to trigger distress or loss of control. Mindfulness of movement was trained as a coping strategy in a pilot study with MS (Mills & Allen 2000).

Summary points for psychological intervention

- Cognitive dysfunction can affect up to half of the people living with MS, and it is an essential factor determining the quality of life. Reduction in processing speed is a common feature in the cognitive profile of MS patients.
- Depression is the most common mental state change associated with MS, and the lifetime prevalence of major depression can approach 50%. Patients with MS also may experience generalized psychological distress that does not meet the criteria for a formal psychiatric diagnosis but affects their quality of life.
- Fatigue is one of MS's most common and disabling symptoms, affecting up to 87% of people with the condition. Patients who do not show overt cognitive dysfunction may be at risk—as a result of fatigue—for having cognitive difficulties during their daily lives leading to problems at the workplace or other aspects of daily functioning.
- A consistent association has been found between stressful life events and subsequent exacerbations of MS

Treatment of MS

Neurologists treat first attacks and relapses of MS with high doses of intravenous steroids for 3 to 5 days and tapering doses of oral steroids for an additional 1 to 2 weeks. Despite its risks and the lack of definitive studies showing its benefit, steroid treatment seems to shorten the duration of disability, increase a patient's vigor, and provide psychological advantages. Studies have shown that several medications provide modest benefits in reducing the frequency and severity of relapses, lesion accumulation, and hospitalizations.

Treatment with steroids or other medications can complicate cognitive and psychiatric disorders (Patten *et al.* 2005).

Drugs that modulate or suppress the immune system include recombinant human interferon preparations (beta-interferon-1a, beta-interferon-1b, beta-interferon-1a, a polypeptide (glatiramer acetate), and a chemotherapy agent (mitoxantrone).

Psychopharmaceuticals

Patients who experience depression or anxiety may have anxiolytics prescribed. Since suicide rates are relatively high among persons with MS (Livneh & Antonak 1997), psychiatric consultation may also be indicated. Some data suggest a role for sildenafil in women with sexual dysfunction due to multiple sclerosis if other, better-established approaches fail (Xiao *et al.* 2012). The antidepressant clomipramine may also alleviate multiple sclerosis (MS) symptoms, specifically its progressive form (Faissner *et al.* 2017). Gabapentin may relieve pain in patients with multiple sclerosis (Faissner *et al.* 2017). Modafinil is a centrally acting agent with sympathomimetic properties that is structurally and pharmacologically different from stimulant medications. It is a wakefulness-promoting agent that is FDA approved to treat fatigue associated with multiple sclerosis (Littleton *et al.* 2010).

Depression

Depression and mood disturbances are cured with antidepressants, antimanic agents, support groups, and psychotherapy (Mohr *et al.* 2001).

Given the burden of depression in MS, antidepressant medication in this population is expected. However, evidence for the efficiency of antidepressants is less clear. As of 2000, only one double-blind, placebo-controlled trial of antidepressant medication, desipramine, and several open-label trials of various selective serotonin reuptake inhibitors (SSRIs) have been published (Gill & Hatcher, 2000). The decision about which antidepressant to use is governed mainly by tolerability concerns. Given the tendency of MS patients to experience a host of neurologically mediated somatic complaints, such as paresis, spasticity, ataxia, impaired balance, incoordination, bladder dysregulation, and sexual dysfunction, the clinician needs to be aware of side effects from the antidepressants. Although SSRIs are the first choice, some patients may better tolerate bupropion, venlafaxine, or mirtazapine. Again, physicians must carefully weigh both the side effect profile and the benefits of each medication. Mirtazapine, although without significant sexual side effects, is associated with sedation that may exacerbate significant fatigue issues related to MS. Tricyclic antidepressants have also demonstrated efficacy in this population. In general, their tolerability is somewhat limited. Given the neurologic morbidity in MS, all psychotropic medications should be used cautiously and individually.

Mania and mixed episodes

Although treatment of manic and psychotic symptoms is not sufficiently established in the MS population, general psychiatry provides some guidance. Valproic acid, lithium, and atypical antipsychotic medications are all indicated. However, case reports suggest that response rates are not robust in individuals with significant CNS lesions (Asghar 2004). Again, side effect profiles are critical. For example, excessive urination—a common side effect of lithium—is poorly matched with bladder dysfunction. For unresponsive mood disorders, electroconvulsive therapy (ECT) is an option. ECT has, however, been associated with promoting MS flare-ups (Mattingley *et al.* 1992).

Valproate is preferable when treating patients with frequently mixed episodes, who have a rapid-cycling course, or who have a so-called secondary mania arising in the context of a medical illness such as MS.

Anxiety disorders

The antipanic effects of valproate have been described in several case reports, which documented successful treatment of panic disorder with MS (Marazziti & Cassano 1996).

Cognitive impairment and dementia

The clinician's first task is often to assess the MS patient's cognitive status. Patients or families may complain of forgetfulness or confusion out of proportion to findings on simple cognitive evaluations. The Folstein Mini-Mental State Examination lacks the sensitivity to identify cognitive morbidity in several circumstances. Neuropsychiatric testing is often helpful in establishing deficits in individual MS patients; however, with no characteristic pattern, specific test results cannot be applied uniformly.

Attempting to ameliorate cognitive deficits in MS tends to focus on compensatory activities. Enhanced structure and strict organization, for example, may reduce some of the disabilities from poor attention and memory. Cognitive rehabilitation, occupational therapy, and psychotherapy may also be effective (Lincoln *et al.* 2020a; b). Immunomodulators, such as interferon beta-1a and interferon beta-1b, may prevent or delay the onset of both neurologic and cognitive disabilities. Studies have also demonstrated improved memory and information processing with these medications. (Early reports that beta-1a caused depression have been refuted (Patten *et al.* 2005). Small studies have shown that the cholinesterase-inhibitor donepezil improved attention, memory, and executive functioning (Greene 2000).

Physical therapy

Individuals with MS should generally remain as active as possible without developing excessive fatigue. Physical therapy may be prescribed to help with mobility problems or use assistive devices, such as walkers, if needed

(Straudi *et al.* 2017; Ziliotto *et al.* 2020; Radecka *et al.* 2021). Specific exercises that decrease calcium loss from bones, strengthen weak muscles, and maintain muscle strength and joint mobility may also be prescribed. Physical therapy that includes massage and passive range-of-motion exercises may also be beneficial. Individuals with MS who experience speech problems may be referred to a speech therapist or use assistive devices, such as a communication board and voice amplifier.

Exercise therapy prevents or treats disorders and chronic disease through regular, repetitive physical activity that enhances fitness and mobility, which robots could assist (Sconza *et al.* 2021). This type of treatment is designed to improve the functional capacity of body structures and has been demonstrated to have beneficial effects for many conditions, such as the alleviation of symptoms of depression and MS (Ziliotto *et al.* 2020)

Limitations of the review

This review has several limitations. First, it was impossible to perform a quantitative synthesis of the results from different articles and studies because of the lack of primary studies and well-conducted randomized clinical trials with a superior level of evidence. Second, potential confounding conditions might affect the view, such as enormous clinical variability and anatomical findings in MS. Last but not least, most studies included were cross-sectional or epidemiological studies rather than randomized controlled trials; a causal relationship cannot be drawn from these types of study design, and these studies are likely to have residual confounding factors.

CONCLUSION

Uncertainty is one of the hallmark characteristics of MS. An initial diagnosis may be hard to grasp for many patients since initial vague and fleeting symptoms are hard to interpret. Unfortunately, uncertainty does not recede over time but does the opposite – leaving patients concerned about which course will their illness take. A neuropsychologically informed psychoeducation, individual or group psychotherapy, and rehabilitation can benefit our patients' treatment regimens as they cope with the losses in adaptive functioning, inefficiencies in cognitive processing, and adverse effects of stress and fatigue on stress neuropsychological status and quality of life. Psychotherapy could assist patients in developing a foundation for living with the losses and uncertainties that accompany a challenging condition such as multiple sclerosis.

CONFLICT OF INTEREST STATEMENT

The authors declare that the article was done in the nonappearance of any commercial or economic relationships that could be understood as a potential conflict of interest.

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