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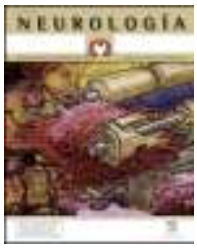

REVIEW ARTICLE

Psychotherapeutic and psychosocial interventions for managing stress in multiple sclerosis: The contribution of mindfulness-based interventions☆,☆☆

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Abstract Depression or anxiety in multiple sclerosis (MS) has been linked to a more severe course of the disease and higher numbers of relapses, in addition to poorer treatment adherence and exacerbated immune system dysregulation. Recent investigations indicate that psychotherapeutic interventions for stress management, such as mindfulness-based interventions (MBIs), could improve quality of life, depression, anxiety, and fatigue in MS patients. Mindfulness fosters the ability to slow down and observe experiences as they truly are, which improves affect regulation. Mindfulness is acquired through training; its advantage over other psychotherapeutic interventions is that effects may remain over time, since cultivating mindfulness depends on regular practising of abilities learned during training. The objective of this article is to review the current evidence of psychotherapeutic and psychosocial interventions, including MBIs for stress management, and their beneficial effects on MS patients.

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Intervenciones psicoterapéuticas y psicosociales para el manejo del estrés en esclerosis múltiple: aportación de intervenciones basadas en mindfulness

Resumen La presencia de depresión o ansiedad asociada al diagnóstico de esclerosis múltiple (EM) se ha relacionado con una peor evolución de la enfermedad, con mayor número de brotes, con peor adherencia al tratamiento y una mayor disregulación del sistema inmune. Estudios recientes indican que intervenciones psicoterapéuticas dirigidas al manejo del estrés, entre ellas, intervenciones basadas en mindfulness (Mindfulness-Based Interventions, MBI), pueden mejorar la calidad de vida, la depresión, la ansiedad y la fatiga en pacientes con diagnóstico de EM. Mindfulness o *atención plena* fomenta la capacidad para observar las experiencias tal y como son y mejora la regulación emocional. Esta habilidad o actitud se aprende por entrenamiento y tiene la ventaja sobre otras intervenciones de que el efecto puede prolongarse a lo largo del tiempo al depender de la práctica personal. El objetivo del presente artículo es revisar la evidencia disponible sobre la eficacia de intervenciones psicosociales y psicoterapéuticas, específicamente MBI, en el manejo de la sintomatología ansioso-depresiva y del estrés percibido en pacientes con diagnóstico de EM.

Introduction

Multiple sclerosis (MS) is a chronic disease with an unpredictable course characterised by inflammation, demyelination, and neurodegeneration of the central nervous system. These processes cause the symptoms of the disease.[1,2] The most common type is relapsing-recurring MS.[3,4] MS is second only to automobile accidents as a cause of disability in younger adults, and it is highly prevalent in Europe (100-200 cases per 100 000 inhabitants), including Spain (70-100 per 100 000). Prevalence is very high in the United States and Canada (up to 300 per 100 000), but low in Sub-Saharan Africa and East Asia, at 2.1 and 2.2 cases per 100 000 inhabitants, respectively.[5,6] The aetiology of the disease is unknown and no curative treatments are currently available. At present, treatment aims to decrease both the number and the severity of exacerbations and lessen the patient's disability. Disease-modifying therapies, which act on the immune system to obtain the results listed above, slow progression of the disease and improve patients' quality of life.[7]

Patients frequently experience depression, fatigue, and cognitive dysfunction, known as the hidden symptoms of MS. Symptoms appear as overlapping comorbidities that are directly associated with markers of inflammation or neurodegeneration.[8] The lifelong prevalence of depression among MS patients is about 50%,[9] compared to 15% in the general population; likewise, the prevalence of anxiety disorders in patients is 25%.[10] A diagnosis of MS is associated with poorer subjective well-being and quality of life,[11] as well as difficulties with social interactions and interpersonal relationships.[12,13] Fatigue, one of the most common symptoms, is present in more than 80% of all patients.[14,15] Furthermore, some 15% to 50% of all patients report that fatigue is associated with increased disability; studies have shown this symptom to be a strong predictor of future incapacity for work.[16,17] Fatigue decreases the patient's quality of life in addition to affecting family and social interactions. Various scales and questionnaires have been validated for measuring quality of life, even though very few drug treatments are able to improve this parameter significantly.[18]

Cognitive dysfunction is characterised by decline in such specific domains as processing speed, attention, memory, executive functions, and learning. Alterations in these areas may be detected by means of sophisticated neuropsychological test batteries even in early stages of MS.[19] In fact, some suggest that neuropsychological dysfunction appearing in the absence of any physical symptoms may be a very sensitive marker of brain damage.[20] Recent studies show that social cognition is often frequently affected, and this manifestation has a negative impact on stress coping mechanisms.[21–23]

Depression may affect the course of MS by decreasing the patient's adherence to treatment and increasing the immune system dysregulation associated with the disease.[24,25] Stress and anxiety have also been linked to a higher frequency of exacerbations, and thus to more numerous demyelinating lesions.[26–32]

Current studies in both human and animal models indicate that, over time, stress may dramatically alter neurobiological mechanisms of homeostasis or control, fundamentally at the level of the neuroendocrine system and stress response systems.[33,34] Emotional distress activates the neuroendocrine stress response systems and provokes an increase in stress hormone secretion.[35] Recent studies also show an association between cytokines and depression. Proposed mechanisms include altered reactivity of the hypothalamic–pituitary–adrenal axis, decreased regulation of serotonin precursors, and impaired neurogenesis.[36–38]

Assessing the efficacy of MS treatments should take into account the social, psychological, and emotional factors included in the concept of 'quality of life'.[39,40] Psychotherapeutic interventions that help reduce patients stress, emotional distress, and fatigue while improving psychosocial

function should be offered routinely as an essential part of MS management.[41,42]

The purpose of this article is to review the psychosocial and psychotherapeutic interventions used in patients with MS, and the effect of these interventions on stress-related parameters. To this end, we used PubMed, Cochrane, and PsychInfo to search for articles on psychotherapeutic, psychosocial, and mindfulness-based interventions (MBIs) and stress management published in the last 10 years. We also considered earlier articles whose results were relevant. References cited by these articles were used to locate other studies. Articles were included in this systematic review according to the following criteria: (1) interventions involving training in psychosocial abilities, psychotherapeutic approaches, or stress management techniques; (2) a study sample partially or completely composed of patients diagnosed with MS.

Psychosocial interventions in multiple sclerosis

Psychosocial interventions are defined as educational or interactive programmes intended to promote healthy behaviours.[43] Physical training programmes are sometimes included among them. However, interventions that facilitate decision-making and interventions for stress management are a better fit in this category, and they have been proved effective for improving quality of life and reducing depression and fatigue.[44–46] Published data indicate that neuropsychological rehabilitation has only a limited ability to recover cognitive losses in MS patients.[47]

Physical training

Physical exercise programmes for patients with MS have shown beneficial effects on quality of life, emotional state, fatigue, and motor function, including walking speed and distance, muscle tone, and coordination.[48–53] The impact of physical exercise on disease progression, specifically the frequency of exacerbations and number of demyelinating lesions, has not yet been thoroughly studied. A single recent study concluded that exercise may affect the course of MS, but data remains scarce.[54]

Psychoeducation and informing patients

The effect of informing patients about the disease was evaluated in a 2014 Cochrane review. That review showed that providing information contributed to better patient awareness of the disease, higher levels of satisfaction with care, and a better quality of life.[55] Only 4 of the 8 studies included in the analysis evaluated behavioural changes in patients,[56–59] and only one study found the intervention to be effective against exacerbations.[60] Patients who attended a 4-hour training session underwent fewer steroid treatments and fewer treatments requiring hospitalisation. They also made fewer calls to their doctors to clarify aspects of treatment management. The most interesting finding of all was that patients attending the training session experienced significantly fewer MS exacerbations than the control group over a 2-year follow-up period.[56]

Cognitive-behavioural interventions

Cognitive-behavioural interventions (CBI) are the psychotherapeutic programmes most likely to be accepted by the scientific community, and those supported by the largest body of empirical research. They have shown their efficacy in treating most mental disorders with a mean treatment effect magnitude of 0.82 compared to non-treatment; this magnitude is similar to that of other widely-used treatments.[61]

Most research on CBI in MS focuses on its effect on symptoms of depression. Randomised controlled clinical trials have shown that CBI is effective for treating depression in patients diagnosed with MS; response to this treatment is equal or superior to that obtained using antidepressants or other interventions.[62,63] Other outcome variables that have been evaluated include use of coping strategies[44] and presence of fatigue[64]; both areas showed improvements after the intervention.

Very few studies have evaluated the effect of CBI on MS progression.[65] Mohr et al. discovered an association between stress and inflammatory activity in brain magnetic resonance imaging (MRI) studies.[30] The same group published the first controlled clinical trial on the effect of a stress-management intervention on demyelinating lesions viewed by MRI.[29] A 24-week course of individual training sessions in stress-management strategies was correlated with a significant decrease in the number of new MRI lesions in test subjects compared to patients on the waiting list. This group also found that a higher percentage of patients remained lesion-free during the intervention period. Nevertheless, the effects disappeared at the end of the intervention. Furthermore, the study could not clarify whether the effects were due to aspects specific to stress management or to other factors, such as the care and social support these patients received.[29] To date, no additional studies exploring these topics have been published.

Online treatments with CBI-based strategies are very attractive since they are easy to access and also able to offer personalised treatment options that optimise professional resources.[66] However, there are no published studies comparing these means of administering CBI to interventions carried out by telephone or in face-to-face individual or group sessions.

Questions about the mechanism definitively responsible for the therapeutic effect of psychotherapeutic interventions in general, and cognitive-behavioural therapy in particular, revolve around whether benefits observed are secondary to changes in behaviour or lifestyle, if they have to do with the patient's receiving more support and attention, or if they stem from alterations in the patient's thought processes and emotions.[43] It is necessary to clarify to what extent cognitive deficit in MS may influence the therapeutic effect of these interventions. Mohr et al. have shown that cognitive impairment and larger demyelinating lesions are associated with poorer ability to maintain the beneficial effects of the intervention once it has come to an end.[67]

Mindfulness-based interventions in multiple sclerosis

Mindfulness is defined as a state of consciousness focusing on the present without interpreting or passing judgement on the situation. The subject focuses on what arises, whether emotions, thoughts, or bodily sensations, while recognising and accepting each of these mental phenomena.[68,69] Practising mindfulness has been recognised as a way of lending conscious attention to the automatic reactions and learned psychological processes that often contribute to emotional imbalance and dysfunctional behaviour.[70] Acceptance and awareness of present experience, and focus on that experience, have been identified as the change processes or action mechanisms that help mitigate emotional distress in those who practise mindfulness.[71]

Mindfulness training is undertaken with the goal of teaching an individual to be fully conscious of what occurs in his or her body and mind (emotions, thoughts, bodily sensations), without this information eliciting either physical or mental reactions.[72] While in a mindful state, an individual may modulate the intensity of memories, decrease reactivity, generate hope, and establish a new identity. An example might be a person with painful memories who does not succumb to his or her pain, fatigue, or physical limitations.

One of the goals of practising mindfulness is training the use of attention. Rather than merely focusing attention, this approach consists of applying relaxed attention (awareness without choice) such that mental phenomena and sensations flow and reach the consciousness, providing a fluctuating experience and insight into the self and reality. Practice increases the individual's ability to distinguish between an experience with all the primary sensations that allow us to perceive it, and the secondary emotional or cognitive reactions that imply judgement (good, bad, indifferent) or an affective quality (pleasant, unpleasant); the latter tend to arise from memories and past experiences. It involves using the mind to its full capacity and living what is happening at each moment as if it were the first time: what are your thoughts, emotions, and bodily sensations at this time? And now? And now? Differentiating between these 2 processing modes facilitates the development of the 'observer ego'.[73,74]

Research shows that continuous attempts at repressing or avoiding thoughts or emotions (common coping strategies) only increase the frequency and intensity of those thoughts and emotions.[75] However, mindfulness increases dispersion of the thought process and changes relationships with those thoughts. When a person is paying attention to a specific focal point, whether breathing, the body, sounds, etc., that person is also aware of the reactions caused by the focus on that point, meaning that the individual observes the attention process, or engages in metacognitive consciousness. The central premise of therapeutic strategies that make use of mindfulness is that the mental state of active metacognitive supervision is able to alter the automatic circuits created by repetitive thought.[76–78]

As with any other psychological ability, mindfulness improves with practice. Mindfulness techniques may be used in association with pharmacological treatment. They may also be one of the main components of a psychotherapeutic intervention such as, for example, mindfulness-based cognitive therapy,[77] mindfulness-based stress reduction (MBSR),[79,80] mindfulness-based narrative therapy (MBNT),[72] dialectical behaviour therapy,[81] and acceptance and commitment therapy.[75,82]

MBIs have become increasingly popular means of managing different aspects of chronic illnesses in the last 30 years.[83] Meditation-based stress reduction (MBSR), designed by Kabat-Zinn, is the intervention that has been featured in the most studies of medical and mental health conditions.[79,80,84,85] Mindfulness training, through MBSR programmes, has been said to elicit neuroendocrine, immunological, and neuroplastic effects, but the nature of these effects has not been studied.[86–89]

The MBSR programme takes place over 8 weeks in group sessions lasting 2.5 hours. Its purpose is to cultivate mindfulness through the practice of meditation and hatha yoga.[90] Each session involves practising the techniques, sharing learning experiences and difficulties, and explaining how psychoeducational interventions affect stress. Reading essays or poems and using metaphors in these sessions is also recommended. Through formal and informal practice, MBSR teaches patients to strengthen their abilities in the following areas: (1) focusing on the present and accepting experiences or thoughts as they arise without trying to control them; (2) exploring the experience by emphasising its emotional and sensory aspects rather than giving a verbal or intellectual description of those aspects; (3) fully accepting the experience, including both positive and negative elements such as feelings of frustration, rage, or uneasiness; (4) actively choosing the experiences to be lived and what elements are to be acted on, focused on, or examined; (5) giving up all pretence of having direct control over reality.[90]

Multiple studies have shown that the MBSR programme is effective for reducing anxiety levels and improving patients' psychological well-being in stressful situations. Patients' stress may arise from a variety of clinical conditions including chronic disease, cancer, MS, and fibromyalgia.[83,91–93]

Published studies of MBIs in MS are scarce. A 2014 review based on results from 3 studies of good methodological quality, with a total of 183 patients, concluded that MBIs could be beneficial. It specifically indicated improvements in quality of life, mental health (anxiety and depression), and certain physical parameters such as fatigue.[83] Grossman et al. published a clinical trial in patients diagnosed with MS in which MBSR was compared to conventional treatment, and reported improvements in quality of life, in addition to lower levels of depression and fatigue.[94] The trial did not include immune function variables, neurocognitive measures, or results from MRI studies. One of its limitations was the absence of comparisons between the mindfulness-based intervention and an active alternative, meaning that the specificity of the intervention cannot be evaluated, and the effects obtained may be the result of non-specific factors. Similar results have been obtained in a recent study of mindfulness-based interventions using Skype in MS patients: this study found improvements in the areas of pain, fatigue, anxiety, and depression in the intervention group compared to controls.[95] Schirda et al. associated the presence of

abilities that can be trained through mindfulness—and requiring no prior training—with less emotional dysregulation and improved quality of life in MS patients. Their hypothesis was that emotional dysregulation could be a key symptom affecting quality of life in these patients, especially those with symptoms indicating high levels of depression.[96] Our study group is preparing a randomised clinical trial that compares mindfulness-based intervention to psychoeducational intervention. In addition to the variables of quality of life, depression, anxiety, and fatigue, we have included immune parameters to evaluate how mindfulness training may affect them.

We do not yet understand the exact relationship between mindfulness practice and the psychological benefits observed in MS patients. Recent studies have linked cognitive dysfunction in MS, fundamentally referring to difficulties with sustained attention and executive function, to unhealthy coping mechanisms.[97,98] Howells et al. have shown that mindfulness-based interventions increase the capacity for attention and reduce interference from irrelevant information. As such, using MBIs may help MS patients promote positive coping mechanisms based on problem-solving strategies.[99]

Another relevant point is that the results from mindfulness training have been linked to improved immune parameters, and immune changes are associated with reductions in depression symptoms and improvements in quality of life.[94] Fang et al. found that patients reporting increased mental well-being after attending an 8-week MBSR programme showed increased NK cell cytolytic activity, whereas those with no increases in mental well-being did not exhibit any changes in NK activity.[100]

Lastly, the beneficial effect of practising mindfulness may be related to the decrease in levels of cortisol, which plays an essential role in modulating stress.[101] In contrast with cognitive-behavioural interventions, which have been shown to have a temporary effect on stress reduction that remains during the course of the intervention,[29] MBIs may have the advantage of an effect that continues over time, since the approach emphasises regular individual practice of learned skills.[102]

Conclusions

MS is a chronic disease with a negative effect on quality of life. Stress may play an important part in the progression of the disease. Psychosocial interventions, particularly MBIs that aim to decrease or manage stress, may be beneficial for patients with MS. They are associated with improvements on measures of quality of life, depression, and fatigue. Future research should evaluate potential changes in immune parameters, as well as any added benefits of these interventions used as adjuvants to different pharmacological treatments. Likewise, cost-utility analyses are needed in order to promote implementing these interventions in our health systems.

Conflicts of interest

The authors have no conflicts of interest to declare.

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