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Review Article

Prevalence of depression and anxiety in Multiple Sclerosis: A systematic review and meta-analysis

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ABSTRACT

Objective: Prevalence rates of depression and anxiety in patients with Multiple Sclerosis (MS) vary widely across studies. Aim of this systematic review and meta-analysis was to a) estimate the prevalence of depression and anxiety in MS, and specifically b) explore sources of heterogeneity (assessment method, prevalence period, study quality, recruitment resource, region) by extensive analyses.
Methods: A computerized search in PubMed, EMBASE, and PsycINFO for studies on depression and anxiety in MS was performed up to December 2014.
Results: Fifty-eight articles with a total sample size of 87,756 MS patients were selected. Pooled mean prevalence was 30.5% (95% CI = 26.3%–35.1%) for depression, and 22.1% (95% CI = 15.2%–31.0%) for anxiety. Prevalence of clinically significant depressive or anxiety symptoms was higher (35% and 34%) compared with disorders (21%; $p = 0.001$ and 10%; $p < 0.001$). Prevalence of a depressive disorder was relatively lower in studies from Europe. Anxiety disorder was more prevalent in community-based samples. Sources of high heterogeneity were not revealed.
Conclusions: Data of a large number of patients indicate increased prevalence of depression and anxiety in MS. Further research is needed to identify sources of heterogeneity. Issues to consider are the definition of depression and anxiety, patient recruitment, and patient characteristics.

Contents

Abbreviations: DSM, Diagnostic and Statistical Manual of Mental disorders; ICD, international classification of diseases; ICPC, international classification of primary care; SCID, structured clinical interview for DSM disorders; CMA, comprehensive meta-analysis; CES-D, center for epidemiological studies depression scale; HADS, hospital anxiety and depression scale; BDI, beck depression inventory; PHQ, patient health questionnaire.

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1. Introduction

Depression and anxiety are common in Multiple Sclerosis (MS) and elevated compared with the general population [1]. Explanations for comorbidity are multifactorial and concern a complex interplay of variables. Depression and anxiety could be natural reactions to the unpredictable course of a disabling and chronic disease. Further, MS patients could be predisposed for depression or anxiety by several psychosocial risk factors such as inadequate coping or insufficient social support, or by MS-related biological processes such as changes in brain structure or in immunological and inflammatory pathways [2–5]. In reverse, depression and anxiety may adversely affect health status by increasing symptom burden, negatively influencing adherence to treatment regimens or by direct pathophysiological effects on immunity [6,7]. Depression and anxiety in MS patients are related to lower quality of life, cognitive dysfunction, elevated suicide risk, and working problems [4,8]. Since depression and anxiety in MS seem to worsen over time and as they are often treatable, early recognition is important and knowledge on their presence and management should be further improved in order to enhance clinical care [4,9–11].

The increased risk of depression or anxiety in MS has often been reported but prevalence rates vary widely from 14% up to 54% [9,12]. This variation could be due to a number of methodological issues, such as differences in definitions, instruments and diagnostic criteria used, and size and nature of the population studied [13]. Often the terms 'depression' and 'anxiety' refer to clinically significant symptoms revealed by self-report scales of different quality, which makes it difficult to compare findings [9,14]. Besides, these scales cannot be used to establish a formal diagnosis of psychiatric disorders and tend to overestimate prevalence rates as compared with diagnostic interviews [13,15]. Further, depressive and anxiety symptomatology in MS has frequently been studied in small MS samples attending MS-clinics or in inpatient settings, underrepresenting patients who are coping well in the community [1,16,17].

A systematic review pooling data from population-based studies showed that depression and anxiety both affect >20% of the MS population [14]. Although the authors performed sensitivity analyses and focused on high quality studies, a high degree of heterogeneity was observed. This implied that prevalence rates varied considerably between the included studies, hampering solid conclusions for the MS population. It is therefore clearly of interest to determine the causes of this heterogeneity as is also suggested by the Cochrane Handbook [18]. This has, to the best of our knowledge, not been previously performed. In addition to revealing the sources of heterogeneity and improving prevalence estimates, it might also offer explanations for the elevated prevalence rates in MS.

In this systematic review and meta-analysis, we therefore aimed to provide a targeted analysis of studies on the prevalence of depression and anxiety in MS and 1) estimate the prevalence of depression and anxiety in MS, and in addition 2) explore sources of heterogeneity by performing subgroup analyses. We evaluated whether the average prevalence estimates varied in relation to a) different definitions of depression and anxiety (disorder vs clinically significant symptoms); b) various methods of assessment and prevalence period; c) quality of research papers; d) patient recruitment resources; and e) different regions. By exploring the heterogeneity by conducting subgroup analyses, we strived to obtain a more comprehensive view on the prevalence of depression and anxiety in MS and its implications for future research.

2. Materials and methods

2.1. Search strategy

A systematic computerized search in PubMed, EMBASE, and Psycinfo was completed in December 2014 for studies on depression and anxiety in Multiple Sclerosis. In collaboration with the librarian, a search strategy was developed which was adjusted correspondingly for each of the databases: The medical subject headings (MeSH) terms 'Depression', 'Depressive Disorder', 'Depressive', 'Anxiety', 'Anxiety Disorders', 'Anxious', 'Emotions', 'Affective Symptoms', 'Mood Disorders', 'Distress', 'Psychological', 'Mental', 'Neurotic' were combined with 'Multiple Sclerosis' and with 'Epidemiology', 'Epidemiologic Studies', and 'Prevalence'. The search was supplemented with a free text word search of these terms (electronic search strategy is displayed in Supplementary material Appendix A).

2.2. Inclusion and exclusion criteria

Studies were included if they met the following criteria: 1) full text publication in English in a peer reviewed journal; 2) a sample size of ≥200 of outpatients with an MS diagnosis, either by self-report or by clinician; 3) report of a depressive or anxiety disorder somewhere during the course of MS by a clinician, identified with (semi) structured interviews based on the Diagnostic and Statistical Manual of Mental disorders (DSM III/IV) [19], the International Classification of Diseases (ICD-9/10) [20] or the International Classification of Primary Care (ICPC) [21] on depressive or anxiety disorders, or clinically significant depressive or anxiety symptoms identified with self-report questionnaires with appropriate psychometric quality (no sub-scales or self-report diagnosis); and 4) provision of sufficient information to calculate prevalence rates e.g. sample size and number or percentages of depressed or anxious patients. We excluded studies with errors in the calculation or presented results, patients under the age of 16 years, studies merely including patients with Clinical Isolated Syndrome or inpatients, and studies with epidemiologically selective samples such as case report