PAPER

A population-based study of depressive symptoms in multiple sclerosis in Stockholm county: association with functioning and sense of coherence

K Gottberg, U Einarsson, S Fredrikson, L von Koch, L W Holmqvist

J Neurol Neurosurg Psychiatry 2007;78:60–65. doi: 10.1136/jnnp.2006.090654

See end of article for authors' affiliations

Correspondence to: K Gottberg, Department of Neurology, R54, Karolinska University Hospital, Huddinge, S-141 86 Stockholm, Sweden; Kristina.Gottberg@ki.se

Received 13 February 2006

Revised 29 June 2006

Accepted 2 July 2006

Published Online First 17 July 2006

Few population-based studies of depression have been conducted on multiple sclerosis,^{1–5} although many reports of depression and its correlation with numerous variables in clinical samples of people with multiple sclerosis (PwMS) have been published. The population-based studies have all reported a high prevalence of depression^{1–5} despite using different methods of data collection.

Depressive symptoms are reported to be associated with decreases in functioning.⁶ In multiple sclerosis, it has been reported that depressed PwMS perform worse than the non-depressed in evaluations of cognitive function,⁷ but there are conflicting reports.⁵ Depressive symptoms in PwMS are also associated with worse self-reported functioning and health-related quality of life scores,⁸ and depressed PwMS have been shown to be more likely to perceive their disability as being greater than their doctors' perception.⁹ It is therefore important to consider different aspects of functioning when evaluating the presence of depression in PwMS.

In the salutogenic model, proposed by Antonovsky,¹⁰ health is described as a continuum between ease and disease rather than as the binary opposite of disease; the model is thus appropriate for studying people afflicted with chronic disorders. Sense of coherence (SOC) refers to "general resistance resources"—capacities that facilitate coping with stressors and thereby improve health.¹⁰ The SOC describes the degree to which a person views the world as meaningful, comprehensible and manageable.¹⁰ SOC has been studied in several patient groups^{11–12} including those with multiple sclerosis.^{13–14} Weak SOC has been found to be associated with a higher prevalence of depression in studies of people with chronic diseases, such as rheumatoid arthritis,¹⁵ but this has not been explored in PwMS.

Certain inconsistencies were observed in previously presented results on depression and its association with

Objectives: To explore and analyse the prevalence of depressive symptoms in people with multiple sclerosis (PwMS), taking into account disease-related and sociodemographic factors, and also to analyse the association between depressive symptoms and functioning (tested and self-reported) and sense of coherence (SOC), respectively.

Methods: Home visits were made to a population-based sample of 166 PwMS. Data were obtained from structured, face-to-face interviews using the Beck Depression Inventory (BDI), the Sickness Impact Profile (SIP) and the SOC scale. A range of tests were also carried out for analyses of different aspects of functioning such as cognitive function, walking capacity and manual dexterity, and structured interviews examined activities of daily living and frequency of social/lifestyle activities.

Results: 19% (28/149) of the people were depressed (BDI ≥ 13). Depressive symptoms were associated with worse self-reported functioning on the SIP and with poor memory function, but not with any of the other tests of functioning. Depressive symptoms were associated with weak SOC, but not with any of the disease-related or sociodemographic factors studied.

Conclusion: The prevalence of depressive symptoms in a population-based sample of PwMS is high. Given the serious nature of depression and its association with worse self-reported functioning and weak SOC, attention to, and treatment of, mental-health problems and depression are strongly indicated in the clinical management of multiple sclerosis.

disease-related and sociodemographic factors.^{1–5} On account of differences in healthcare systems and policies, the results from population-based studies of depression and functioning in other countries may not easily be extrapolated to Swedish conditions.

We have conducted a cross-sectional, population-based study of PwMS in Stockholm county, to comprehensively describe and analyse their functioning and health (the Stockholm MS Study). In this report from the Stockholm MS Study, the aim was to explore the prevalence of depressive symptoms, taking into account disease-related and sociodemographic factors, and also to analyse the association between depressive symptoms and functioning (tested and self-reported) and SOC, respectively.

MATERIALS AND METHODS

The case findings of the PwMS included in this study have previously been described in detail.¹³ A random sample representing 15% ($n = 321$) of the population was taken from a temporary data pool consisting of lists of presumptive cases from hospitals where PwMS are diagnosed and treated ($n = 2129$). A validation was carried out of lists of cases from nursing homes in one municipality of Stockholm county and from private neurologists in the area, and all cases were found in the temporary pool. After perusal of the medical records by the treating neurologists, and of the records of the Swedish National Population Registry, it was determined that 122 PwMS failed to fulfil our inclusion criteria (fig 1). In all, 166 (85%) PwMS gave informed consent and agreed to participate.

Abbreviations: ADL, activities of daily living; BDI, Beck Depression Inventory; PwMS, people with multiple sclerosis; SIP, Sickness Impact Profile; SDMT, Symbol Digit Modalities Test; SOC, sense of coherence

Figure 1 Flow chart showing the case-finding procedure and the inclusion criteria for the study. MS, multiple sclerosis.

Procedure

Data were obtained using structured face-to-face interviews during home visits to PwMS by a clinically experienced nurse or a physiotherapist (KG, UE). These interviews lasted up to 2½ h and were carried out using a comprehensive evaluation package in a standardised order, a method that has previously been evaluated and found to be feasible.^{16–17} Information on disease-related characteristics, sociodemographic factors and current type of symptomatic treatment, including psychotropic drugs, was collected through the interview with the PwMS.

Questionnaires and tests

Information on depressed mood was collected using the Beck Depression Inventory (BDI).¹⁸ The questionnaire consists of 21 items that add together to give a total BDI score ranging from 0 to 63 points. Each item scores from 0 to 3. PwMS in the sample with BDI scores ≥ 13 ^{19–20} were classed as depressed. In subgroup analyses, however, BDI cut-off scores of both 13 and 10¹⁸ were used.

Cognitive function was evaluated using the Symbol Digit Modalities Test (SDMT)²¹ and the free recall portion of the Free Recall and Recognition of 12 Random Words Test.²² Walking capacity was evaluated by timing of rapid walking over a distance of 5×2 m.^{23–24} The use of walking aids was noted, and the inability to walk was set at 0 m/s. Manual dexterity was evaluated using the Nine-Hole Peg Test,²⁴ measuring pegs per second, and inability to perform the Nine-Hole Peg Test was set at 0 pegs/s. Activities of daily living (ADL) were evaluated using the Barthel Index²⁵ and the Katz-Extended ADL Index.²⁶ The frequency of social or lifestyle activities was evaluated using the Frenchay Activities Index.²⁷ Self-reported functioning was evaluated by the Sickness Impact Profile (SIP),^{28–29} using total score, physical and psychosocial dimension, and scores of the 12 subcategories.

To analyse sense of coherence, the short Swedish version³⁰ of the SOC scale³¹ was used. The questionnaire consists of 13 items with answers rated on a Likert scale from 1 to 7. The total score ranges from 13 to 91.

Table 1 describes the cut-off levels used for categorisation of performance below normal cognitive function,^{21–22} walking capacity,²³ manual dexterity,²⁴ independence in ADL, frequency of social or lifestyle activities below normal,²⁵ and weak SOC.³⁰ Regarding SOC scores, the PwMS were compared with a Swedish reference population³⁰; scores within the lowest reference quartile were classed as weak SOC, and scores above

the lowest reference quartile were classed as moderate to strong SOC.

PwMS were classified into the following four disease-severity subgroups: mildly disabled (0–3.0), moderately disabled (3.5–5.5), severely disabled (6.0–6.5), and very severely disabled (≥ 7.0), according to the Expanded Disability Status Scale,³⁶ on the basis of home evaluation, and were verified by a senior neurologist (SF) after, but in association with, the home visit. PwMS were further classified into groups with disease duration shorter or longer than 10 years and into disease courses of relapsing remitting, secondary progressive or primary progressive multiple sclerosis. PwMS were also classified into socio-demographic subgroups according to sex, living with partner or alone, type of housing (private/sheltered accommodation), level of education (basic/university level education) and work status (working/not working). In subgroup analysis of work status, PwMS who were retired because of their age were excluded.

Statistical methods

For comparisons of groups, Student's *t* test was used for continuous data (walking speed, pegs/s on the Nine-Hole Peg Test) and the Mann-Whitney *U* test or the Kruskal-Wallis test for ordinal data (eg, ADL and the SIP). For analyses of categorical data (eg, dependent or independent in ADL, depressed or non-depressed), a χ^2 test or Fisher's exact test was used. A regression analysis was used with the two cognitive variables entered at step 1, SOC at step 2, and the interaction term of SOC and the cognitive variables, respectively, at step 3, testing the possibility of SOC moderating the relationship between cognitive dysfunction and depressive symptoms. To account for multiple comparisons, probability values ≤ 0.01 were considered significant.

All data were analysed using SPSS V.13.0.

Ethical approval for the study was obtained from the Ethics Committee of Karolinska University Hospital, Huddinge, Sweden.

RESULTS

Table 2 presents the sociodemographic and disease-related characteristics of the 166 PwMS. The mean age was 51 years and 71% were women. Eighteen PwMS (11%) had been prescribed symptomatic treatment for depression (sertraline, paroxetine, citalopram or mirtazapine). One PwMS had amitriptyline prescribed for central neurogenic pain.

In all, 149 PwMS completed the BDI interview. The mean (SD) BDI score of these PwMS was 8 (6) and the median

Table 1 Cut-off levels used for categorisation of performance below normal cognitive function, walking ability, manual dexterity, dependency in activities of daily living, frequency of social or lifestyle activities below normal and sense of coherence

Variable	Questionnaire/instrument	Criteria
Cognitive function	Symbol Digit Modalities Test Free recall portion of the Free Recall and Recognition of 12 Random Words Test	Age-related norms, written or oral reply, -1.5 SD ²¹ Age-related/sex-related norms, -1 SD ²²
Walking ability	Walking speed 10 m (5×2)	Age-related/sex-related norms, -1 SD ³³
Manual dexterity	Nine-Hole Peg Test	<0.5 pegs/s ³⁴
ADL	Barthel Index Katz-Extended ADL Index	<100 Dependent in one or more items
Frequency of social or lifestyle activities	Frenchay Activities Index	Age-related/sex-related norms, $<$ lower quartile ³⁵
SOC	Sense of coherence scale	Weak SOC: 13–54 points; moderate–strong SOC: 55–91 points ³⁰

ADL, activities of daily living.

(interquartile range) score was 7 (3–12). In all, 28 (19%) people were depressed (BDI ≥ 13). The five most commonly reported items were fatigability (82%), loss of libido (54%), sleep disturbance (51%), difficulty working (46%) and irritability (46%; fig 2). The proportion who reported use of antidepressant drugs was 5 of 28 (18%) among the depressed PwMS and 12 of 121 (10%) among the non-depressed.

Six PwMS could not participate in the BDI interview because of severe depressive symptoms as clinically evaluated at the home visit. Other reasons for not completing the BDI interview were cognitive dysfunction or a combination of several reasons. Higher percentages of PwMS who did not complete the BDI interview lived in sheltered accommodation, and more often had severe disease and secondary progressive multiple sclerosis than PwMS who completed the interview. Non-participating PwMS also had worse functioning than participating PwMS for all measures used.

Regardless of whether we used a BDI cut-off score of 10 or 13 (whereby, respectively, 59 and 28 of 149 PwMS were classed as depressed), there were no significant differences between

depressed and non-depressed PwMS in terms of percentage with cognitive dysfunction (SDMT), walking ability or manual dexterity below normal; percentage dependent in ADL; or percentage with frequency of social or lifestyle activities below normal. With a BDI cut-off score of 13, a higher proportion of PwMS with memory function below normal according to the Free Recall and Recognition of 12 Random Words Test was found among the depressed (29%) than among the non-depressed (9%; $p = 0.005$).

In analyses with functioning measures used continuously, depressed PwMS did not perform significantly worse than non-depressed in tests of cognitive function, walking ability and manual dexterity or self-reported ADL, and frequency of social or lifestyle activities.

Depressed PwMS (BDI ≥ 13) had worse SIP scores mostly in the psychosocial categories (table 3). In addition, depressed PwMS (according to BDI ≥ 10) had worse self-reported functioning in the SIP categories mobility and ambulation (table 3).

Higher percentages of depressed PwMS were found among those with weak SOC than among those with moderate to strong SOC (using BDI ≥ 13 ; 53% v 15%, $p < 0.001$). In regression analyses, SOC did not moderate the relationship between

Table 2 Sociodemographic and disease-specific information and sense of coherence of the sample of people with multiple sclerosis in Stockholm (n = 166)

Variable	PwMS, n (%)
Age when surveyed (years)	51 (12)* (19–79)†
Women/men	118/48 (71/29)
Living with a partner	102 (61)
Type of housing/sheltered accommodation	11 (7)
University level education	66 (40)
Working	68 (41)
Swedish origin	151 (91)
Age at disease onset (years)	31 (10)* (11–58)†
Disease duration (years)	19 (11)* (1–55)†
Disease severity (EDSS)	
Mild (0–3)	42 (25)
Moderate (3.5–5.5)	35 (21)
Severe (6–6.5)	47 (28)
Very severe (>7)	42 (25)
Disease course	
Relapsing/remitting	70 (42)
Secondary progressive	80 (48)
Primary progressive	16 (10)
Ongoing pharmacological treatment when surveyed	
Disease modifying	68 (41)
Symptomatic treatment	129 (78)
Antidepressants	18 (11)
Weak sense of coherence‡	15 (10)

EDSS, Expanded Disability Status Scale; PwMS, people with multiple sclerosis.

*Mean (SD).

†Range.

‡n = 145.

Figure 2 Percentages of people with multiple sclerosis who received a score of 1–3 on the Beck Depression Inventory items (n = 149).

Table 3 Median (interquartile range) Sickness Impact Profile scores in depressed and non-depressed people with multiple sclerosis (n = 149) in Stockholm

Variable	Depressed BDI ≥ 13	Non-depressed BDI < 13	p Value	Depressed BDI ≥ 10	Non-depressed BDI < 10	p Value
SIP total score	29 (22–37)	20 (10–29)	0.001	28 (18–34)	17 (7–28)	0.001
SIP physical dimension	28 (12–40)	21 (8–35)	0.222	28 (13–43)	20 (4–34)	0.018
SIP psychosocial dimension	24 (15–35)	10 (5–20)	< 0.001	21 (14–29)	8 (3–14)	< 0.001
Sleep and rest	35 (21–51)	22 (10–34)	0.005	34 (21–46)	19 (10–34)	< 0.001
Emotional behaviour	28 (19–47)	10 (0–21)	< 0.001	25 (11–43)	0 (0–11)	< 0.001
Body care and function	22 (12–37)	17 (5–41)	0.436	22 (11–41)	15 (2–37)	0.045
Home management	39 (20–65)	41 (8–63)	0.368	43 (21–67)	34 (0–58)	0.044
Mobility	22 (8–32)	11 (0–25)	0.042	17 (9–27)	6 (0–25)	0.004
Social interactions	18 (11–34)	7 (0–17)	< 0.001	17 (7–25)	5 (0–12)	< 0.001
Ambulation	31 (23–29)	26 (13–40)	0.119	31 (24–49)	24 (10–40)	0.004
Alertness behaviour	29 (9–68)	10 (0–29)	0.004	29 (10–53)	10 (0–21)	< 0.001
Communication	15 (0–31)	10 (0–20)	0.111	10 (0–21)	9 (0–19)	0.087
Work	70 (26–70)	26 (7–70)	0.014	45 (8–70)	27 (8–70)	0.610
Recreation and pastimes	38 (22–49)	30 (19–44)	0.048	32 (22–49)	29 (9–41)	0.016
Eating	5 (0–8)	0 (0–10)	0.544	5 (0–11)	0 (0–6)	0.147

BDI, Beck Depression Inventory; SIP, sickness impact profile.

cognitive dysfunction (SDMT or Free Recall and Recognition of 12 Random Words Test) and depressive symptoms significantly.

Depressive symptoms were equally common among PwMS in different disease severity groups ranging from mild to very severe, among those with shorter and longer disease duration, and among those with a relapsing remitting, secondary progressive or primary progressive disease course. Depressive symptoms were also equally common in men and women, in PwMS living with a partner or living alone, in PwMS living in a private household or in sheltered accommodation, in PwMS with basic or higher education, and in PwMS who were working or not working.

DISCUSSION

We have found that the prevalence of depressive symptoms was 19% in this population-based sample of PwMS in Stockholm, with the BDI cut-off score ≥ 13 .¹⁹ Furthermore, only 11% reported current antidepressant use. The most commonly reported symptom was tiredness. Depressive symptoms were associated with many dimensions of self-reported functioning on the SIP, mainly those of psychosocial character. Depressed PwMS performed worse in the memory function test than the non-depressed, but not in any of the other tests of functioning (walking speed, manual dexterity and attention by the SDMT or in measures of ADL and lifestyle activities). Furthermore, depressive symptoms were associated with weak SOC but not with any of the sociodemographic or disease-related factors.

Depressive symptoms are common in the normal population, which is illustrated by the fact that at any particular time, 4–10% of the adult population meet the criteria for a depressive episode.³⁷ In a previous report from the Stockholm MS Study, presenting EuroQol-5D data of the same study population,¹⁴ 46% of PwMS reported moderate or severe problems of anxiety or depression, which was a significantly higher proportion than in the age-matched controls living in Stockholm. The results of the present study with 40% depressed PwMS (with the traditional BDI cut-off score ≥ 10 for minimal depression¹⁸) is a similar but lower proportion, and thus does not seem to be overestimated. The proportion found is in line with the population-based study by Chwastiak *et al.*,³ who found a prevalence of 42% for clinically depressive symptoms in PwMS, using another self-reporting depression questionnaire sent by mail.

The proportion of PwMS who reported ongoing use of antidepressant drugs was surprisingly low. The reason for this finding is unclear. To what extent the PwMS in this Stockholm

study were using antidepressant management strategies other than drugs, such as psychotherapy, is not known.

In this study, we found that PwMS with depressive symptoms did not perform worse in different aspects of functioning, such as in tests of walking and manual dexterity. By contrast, when PwMS were questioned about different aspects of functioning in structured interviews using the SIP, depressed PwMS (BDI ≥ 10) reported worse functioning in terms of ambulation, mobility, sleep and rest, emotional behaviour, social interactions and alertness behaviour. The SIP captures, for example, other dimensions of walking abilities (walking downhill and uphill, climbing stairs and usual walking behaviour) than walking speed alone. Therefore, the lack of differences seen in results of the more objective measures of functioning may be related to the lack of sensitivity of the measures—to their tendency to underestimate disability in depressed and non-depressed PwMS alike. The sample size in the study limited the statistical power for detecting differences among certain subgroups, and the choice of 0.01 as the level below which probability values were considered significant was certainly justified given the high number of analyses. Future studies should continue to analyse the effect of depressive symptoms on functioning,⁹ from both an observer's perspective and the perspective of PwMS and using the same variables.

In a population-based study of depressive disorders in Stockholm,³⁸ depressed people showed impairments in tasks requiring episodic memory, but the pattern of impairments varied with the type of depression (major and minor depression, dysthymia, etc). In our sample of PwMS, we found that poor memory function was significantly associated with depressive symptoms (BDI ≥ 13). Other studies have also found this relationship, and it has been suggested that depression adversely affects working memory.³⁹ As suggested in the literature, these associations are probably bidirectional, and cannot be identified in a cross-sectional design. Voss *et al.*⁴⁰ conducted a study in PwMS and hypothesised that a disease will lead to a depressive effect only if it disrupts physical or psychosocial functioning. They found that fatigue and physical disability were indirectly and directly predictive of depression through their effects on recreational functioning. Bearing in mind our results, we therefore acknowledge that depression in PwMS must not be seen as an isolated manifestation or symptom but in relation to the individual life situation, taking into consideration many aspects of health and functioning.

To our knowledge, this is the first study to present results of the association between depressive symptoms and sense of

coherence in multiple sclerosis. Most PwMS in the study (90%) were categorised as having moderate to strong SOC, indicating that many of them view life as meaningful, comprehensible and manageable¹⁰ despite living with multiple sclerosis. Higher proportions of depressed PwMS were found among those with weak SOC than among those with moderate to strong SOC, supporting the notion that strong SOC may act as a protective factor against depressive symptoms.¹⁵ However, as this study is cross-sectional, no conclusion about causal relationships can be drawn. Longitudinal studies of depressive symptoms and sense of coherence are therefore warranted.

In this study, we found no significant differences in the proportions of depressed PwMS within disease-related or sociodemographic subgroups. These results differ in some respects from other population-based studies of depression,^{1–5} and may partly depend on differences in the socioeconomic or cultural context and methods of data collection. An example of different results among these studies is the issue of sex, with depression reported as being higher in women than in men,^{1,2} higher in men than in women,⁴ and also as having a similar prevalence among men and women (as in the present study).³ In an Irish population-based study similar to ours,⁵ using the BDI, no association was found between signs of depression and sociodemographic or disease-specific factors, apart from PwMS with a shorter mean disease duration having more signs of depression.

BDI is one of the most frequently used questionnaires for assessing depression³⁷ and was recently recommended for use in populations with multiple sclerosis for clinical purposes to identify those PwMS who may merit special attention and follow-up.¹⁹ Several cut-off scores for depression using the BDI have been suggested in the literature. On using the cut-off score of 13 as recommended by the Goldman consensus group on depression,¹⁹ 19% of PwMS were found to have depression. Sullivan *et al*²⁰ studied BDI results of newly diagnosed PwMS and found that using a cut-off score of 13 resulted in a sensitivity of 0.71, implying that about 30% of PwMS who are depressed have BDI scores <13. We believe that 30% is a rather large proportion to leave undetected if the goal is to optimise physical and mental health in PwMS. Predictably, in population-based studies,³ the proportion of PwMS classified as depressed decreases when higher cut-off scores are used. This implies that many PwMS who do not fulfil more stringently defined criteria for moderate to severe depression may nevertheless show clinically significant depressive symptoms and be in need of medical attention and follow-up for their problems. As in many other studies of depressed mood in PwMS, it is recognised that physical items are often marked, and that they are difficult to differentiate from symptoms related to multiple sclerosis. Using the full 21-item BDI has been recommended, as all BDI items decreased significantly in a treatment study of psychological and pharmacological interventions for depression.⁴¹

For the most serious item of the BDI—suicidal ideation—9% of PwMS confirmed that they had these thoughts to a certain extent. Suicide has been reported to be more than twice as common among Swedish PwMS as in the general population,⁴² which highlights the importance of identifying PwMS at risk, so that action can be taken as regards the clinical management of multiple sclerosis.

A clinical implication from the results of the present study is to incorporate depressive symptoms or mental health as a standard parameter for assessment and follow-up in clinical MS management. The Swedish Council on Technology Assessment in Health Care has undertaken a systematic review of the treatment of depression,³⁷ and concludes that there are a large number of antidepressants and several types of

psychotherapy that have been shown to be effective for treating major depression in adults. Although depression is frequently studied in multiple sclerosis, few randomised clinical trials have been conducted to study outcomes of different psychological interventions or antidepressant treatments for depression. Besides psychopharmacological or psychological interventions, the effects of individualised management of multiple sclerosis, rehabilitation and physical activity on depression should also be further studied.

This is the first study in Sweden to describe the presence of depressive symptoms in a population-based sample of PwMS, with the strengths of using face-to-face interviews and tests at home visits. This study does have some limitations, however. As it did not aim to assess the prevalence of depressive symptoms compared with the general population, but rather to assess its prevalence according to an instrument included in an evaluation package of functioning, no control group was available. Furthermore, the proportion of PwMS treated with disease-modifying drugs was high compared with the average proportion seen in Sweden at the time of the study,⁴³ and the prevalence of fatigue was not specifically assessed in the study, other than in the sleep and rest category of the SIP.

Conclusion

The prevalence of depressive symptoms in a population-based sample of PwMS is high, regardless of factors such as sex or disease severity. In view of this fact, and of the serious nature of depression and its association with worse self-reported functioning and weak SOC, attention to, and treatment of, mental-health problems and depression are strongly indicated in the clinical management of multiple sclerosis.

ACKNOWLEDGEMENTS

We thank all the PwMS for their participation in this study and also Thomas Masterman, MD, PhD of the Division of Neurology of the Department of Clinical Neuroscience, Karolinska Institutet for his valuable comments on the manuscript.

Authors' affiliations

K Gottberg, S Fredrikson, L von Koch, Division of Neurology, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
U Einarsson, L W Holmqvist, Division of Physiotherapy, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet

Funding: The study was funded by grants from the Swedish Association of Neurologically Disabled; the Swedish Research Council; and the Center for Health Care Sciences at the Karolinska Institutet.

Competing interests: None.

REFERENCES

- 1 Patten SB, Beck CA, Williams JVA, *et al*. Major depression in multiple sclerosis. *Neurology* 2003;**61**:1524–27.
- 2 Patten SB, Metz LM, Reimer M. Biopsychological correlates of lifetime major depression in a multiple sclerosis population. *Mult Scler* 2000;**6**:115–20.
- 3 Chwastak L, Ehde DM, Gibbons LE, *et al*. Depressive symptoms and severity of illness in multiple sclerosis: epidemiologic study of a large community sample. *Am J Psychiatry* 2002;**159**:1862–68.
- 4 Hakim EA, Bakheit AM, Bryant TN, *et al*. The social impact of multiple sclerosis—a study of 305 patients and their relatives. *Disabil Rehabil* 2000;**22**:288–93.
- 5 McGuigan C, Hutchinson M. Unrecognised symptoms of depression in a community-based population with multiple sclerosis. *J Neurol* 2005;**253**:219–23.
- 6 Keller MB. Past, present, and future directions for defining optimal treatment outcome in depression. Remission and beyond. *JAMA* 2003;**289**:3152–60.
- 7 Arnett PA, Higginson CI, Voss WD, *et al*. Depressed mood in multiple sclerosis: relationship to capacity-demanding memory and attentional functioning. *Neuropsychology* 1999;**13**:434–46.
- 8 Benedict RH, Wahlig E, Bakshi R, *et al*. Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behaviour change. *J Neurol Sci* 2005;**231**:29–34.
- 9 Smith SJ. The role of affect on the perception of disability in multiple sclerosis. *Clin Rehabil* 2000;**14**:50–4.

- 10 Antonovsky A. *Unravelling the mystery of health*. San Francisco: Jossey-Bass, 1987:15–32.
- 11 Widén Holmqvist L, von Koch L, Kostulas V, *et al*. A randomized controlled trial of rehabilitation at home after stroke in Southwest Stockholm. *Stroke* 1998;**29**:591–7.
- 12 Richardson A, Adner N, Nordström G. Persons with insulin-dependent diabetes mellitus: acceptance and coping ability. *J Adv Nurs* 2001;**33**:758–63.
- 13 Einarsson U, Gottberg K, von Koch L, *et al*. Cognitive and motor function in people with multiple sclerosis in Stockholm County. *Mult Scler* 2006;**12**:340–53.
- 14 Gottberg K, Einarsson U, Ytterberg C, *et al*. Health-related quality of life in a population-based sample of people with multiple sclerosis. *Mult Scler* 2005;**11**:450–8.
- 15 Buchi S, Sensky T, Allard S, *et al*. Sense of coherence—a protective factor for depression in rheumatoid arthritis. *J Rheumatol* 1998;**25**:869–75.
- 16 Gottberg K, Einarsson U, Fredrikson S, *et al*. Multiple sclerosis in Stockholm County. A pilot study of utilization of health-care resources, patient satisfaction with care, and impact on family caregivers. *Acta Neurol Scand* 2002;**106**:241–7.
- 17 Einarsson U, Gottberg K, Fredrikson S, *et al*. Multiple sclerosis in Stockholm County. A pilot study exploring the feasibility of assessment of impairment, disability and handicap by home visits. *Clin Rehabil* 2003;**17**:289–98.
- 18 Beck AT, Ward CH, Mendelson M, *et al*. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;**4**:561–71.
- 19 Goldman Consensus Group. The Goldman Consensus statement on depression in multiple sclerosis. *Mult Scler* 2005;**11**:328–37.
- 20 Sullivan MJL, Weinshenker B, Mikail S, *et al*. Screening for major depression in the early stages of multiple sclerosis. *Can J Neurol Sci* 1995;**22**:228–31.
- 21 Smith A. Symbol Digit Modalities Test (SDMT). In: Lezak MD, eds. *Neuropsychological assessment*. 3rd edn. Oxford: Oxford University Press, 1995:379–81.
- 22 Wahlén A. *Episodic memory functioning in very old age. Individual differences and utilization of cognitive support* [dissertation]. Stockholm: Karolinska Institutet, 1996.
- 23 van Herk IE, Arendzen JH, Rispens P. Ten-metre walk, with or without a turn? *Clin Rehabil* 1998;**12**:30–5.
- 24 Rudick R, Antel J, Confavreux C, *et al*. Recommendations from the National Multiple Sclerosis Society Clinical Outcomes Assessment Task Force. *Ann Neurol* 1997;**42**:379–82.
- 25 Mahoney FI, Barthel DB. Functional evaluation: the Barthel Index. *Md State Med J* 1965;**14**:61–5.
- 26 Hulter Åsberg K, Sonn U. The cumulative structure of personal and instrumental ADL. *Scand J Rehabil Med* 1989;**21**:171–7.
- 27 Wade D, Legh-Smith L, Langton Hewer R. Social activities after stroke: measurement and natural history using Frenchay Activities Index. *Int Rehabil Med* 1985;**7**:176–81.
- 28 Bergner M, Bobbitt RA, Carter WB, *et al*. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care* 1981;**19**:787–805.
- 29 Sullivan M, Ahlmen M, Archenholtz B, *et al*. Measuring health in rheumatic disorders by means of a Swedish version of the sickness impact profile. Results from a population study. *Scand J Rheumatol* 1986;**15**:193–200.
- 30 Langius A, Björvell H. Coping ability and functional status in a Swedish population sample. *Scand J Caring Sci* 1993;**7**:3–10.
- 31 Antonovsky A. The structure and properties of the sense of coherence scale. *Soc Sci Med* 1993;**36**:725–33.
- 32 Backman L, Forsell Y. Episodic memory functioning in a community-based sample of old adults with major depression: utilization of cognitive support. *J Abnorm Psychol* 1994;**103**:361–70.
- 33 Oberg T, Karsznia A, Oberg K. Basic gait parameters: reference data for normal subjects, 10–79 years of age. *J Rehabil Res Dev* 1993;**30**:210–23.
- 34 Heller A, Wade DT, Wood VA, *et al*. Arm function after stroke: measurement and recovery over the first three months. *J Neurol Neurosurg Psychiatry* 1987;**50**:714–19.
- 35 Turnbull JC, Kersten P, Habib M, *et al*. Validation of the Frenchay Activities Index in a general population aged 16 years and older. *Arch Phys Med Rehabil* 2000;**81**:1034–8.
- 36 Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983;**33**:1422–27.
- 37 The Swedish Council on Technology Assessment in Health Care. Treatment of depression. A systematic review. Summary and conclusions. <http://www.sbu.se> (accessed 5 September 2005).
- 38 Airaksinen E, Larsson M, Lundberg I, *et al*. Cognitive functions in depressive disorders: evidence from a population-based study. *Psychol Med* 2004;**34**:83–91.
- 39 Arnett PA, Higginson CI, Voss WD, *et al*. Depression in multiple sclerosis: relationship to working memory. *Neuropsychology* 1999;**13**:546–56.
- 40 Voss WD, Arnett PA, Higginson CI, *et al*. Contributing factors to depressed mood in multiple sclerosis. *Arch Clin Neuropsychol* 2002;**17**:103–15.
- 41 Moran PJ, Mohr DC. The validity of Beck Depression Inventory and Hamilton Rating Scale for depression items in the assessment of depression among patients with multiple sclerosis. *J Behav Med* 2005;**28**:35–41.
- 42 Fredrikson S, Cheng Q, Jiang GX, *et al*. Elevated suicide risk among patients with multiple sclerosis in Sweden. *Neuroepidemiology* 2003;**22**:146–52.
- 43 Andersson A, Persson PM, Fredrikson S. Place of residence determines access to interferon-beta therapy in MS. (Less than 15 per cent of patients are treated – big differences between the counties) (in Swedish). *Lakartidningen* 1999;**96**:5492–95.