PAPER

The outcome of depressive disorders in neurology patients: a prospective cohort study

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Background: In a previous prospective study of 300 consecutive new attenders at neurology outpatient clinics, depressive disorders were diagnosed in 119 patients (40%) and major depressive disorder in 77 (26%).
Objective: To describe the eight month outcome of depression in this cohort.
Methods: Patients were reinterviewed eight months after their baseline assessment. Mental state was examined using the primary care evaluation of mental disorders (PRIME-MD) interview and the hospital anxiety and depression (HAD) self rating scale. Health status was measured using the medical outcome study 36 item short form scale (SF-36).
Results: Of the original cohort of 300, 226 (75%) participated in the follow up. Among them, 88 had a depressive disorder at baseline and 69 (78%) of those were still depressed at follow up; 54 had major depression at baseline and 46 (85%) of those still had a major depressive disorder at follow up. Among the 138 patients who had no depression at baseline, 20 new major depressive disorders had developed by the time of follow up. Resolution of major depressive disorders was associated with an improvement in health status.
Conclusions: Most depressive disorders detected in neurology outpatients persist at an eight month follow up, and a substantial number of new cases arise. Resolution of depressive disorders, particularly major depressive disorder, is associated with an improvement in health status.

The coexistence of depression with neurological disorders has long been recognised. In a previously published report of 300 consecutive new attenders at neurology outpatient clinics, we identified 119 patients (40%) who had a depressive disorder.[1] We also found a strong association between the presence of depression and decreased health status, including physical, social, and work related functioning. We concluded that depression was an important contributor to the morbidity of neurology patients. However, before arguing that depression should be a target for intervention in such patients we also need to know whether depression present at the time of assessment persists[2] and whether changes in depression are associated with changes in health status.

In this paper, we describe an eight month follow up study of the same 300 patients which addresses these points. The specific questions asked were as follows. How many patients had a depressive disorder eight months after their initial visit to the neurology clinic? In how many of those depressed at follow up had the depressive disorder been present at baseline assessment, and in how many was it new? Was a change in depression status (that is, depressive disorder to no depression, or no depression to depressive disorder) associated with a change in functional status, and if so was this associated with a change in the neurological condition?

METHODS

The initial study has been described in detail elsewhere.[1] In brief, we interviewed a consecutive sample of 300 newly referred general neurology outpatients to assess the neurological diagnosis and the presence of depressive disorders, and to determine health status.

Measures

Neurological diagnoses were made by consultant neurologists following their clinical examination and investigations.

Psychiatric diagnoses were made using the primary care evaluation of mental disorders (PRIME-MD),[2] according to the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV) classification.[3] The PRIME-MD is a brief structured interview of proven reliability and validity, which was developed from the structured clinical interview for DSMIII-R (SCID).[4] All patients completed the full interview, and the initial questionnaire—although completed—was not used as an initial screening instrument. The specific diagnoses examined were major depression, partial remission of major depression, minor depression (research criteria, appendix B, DSM-IV), and dysthymia. Patients also completed the hospital anxiety and depression scale (HAD),[5] a self rated scale designed for use in patients who have co-morbid physical illness. We used the HAD total score as a continuous measure of depression severity.

Health status was measured with the medical outcome study 36 item short form scale (SF-36).[6] This widely used self report scale measures health status in eight domains: general health perceptions, physical functioning, physical role functioning, bodily pain, social functioning, vitality, mental health, and emotional role functioning.

Follow up assessment

This study was a follow up of the same 300 patients eight months after their baseline assessment. The follow up assessment consisted of a case note review to determine changes in neurological status and a repeat interview with the same measures used in the initial assessment. Interviews were conducted by telephone. When a patient had no telephone, or preferred to see the interviewer, or where there was communication difficulty, a face to face interview was

Abbreviations: DSM, diagnostic and statistical manual of mental diseases; HAD, hospital anxiety and depression scale; PRIME-MD, primary care evaluation of mental disorders; SF-36, medical outcome study 36 item short form scale

Table 1 Diagnoses given to illustrate the case mix (n = 300)*

Headache	63 (21%)
Epilepsy/fits/pseudoseizures	43 (14%)
Multiple sclerosis	30 (10%)
Neuropathies (peripheral/ entrapment)	25 (8%)
Syncope	22 (7%)
Spinal pathology (cervical/ lumbar)	22 (7%)
"Dizziness"	8 (3%)
Parkinson's disease	7 (2%)
Psychiatric diagnosis only	7 (2%)
Other†	73 (26%)

*Diagnoses do not necessarily indicate neurological disease; some are simply symptom descriptions. In 90 patients (30%), symptoms were judged to be predominantly medically unexplained.
†Diagnoses in the "other" category each had a frequency of less than 2%.

conducted. Good agreement between telephone and face to face diagnostic interviews has been reported.[7] The interviews were conducted by AC and KP, both of whom had been trained in psychiatric diagnostic assessment.

The study was approved by the local research ethics committee.

Analysis

First, we compared demographic characteristics and depression status at baseline between those who participated in follow up and those who did not, in order to assess the possibility of systematic bias in the follow up sample.

Second, we described the prevalence of depressive disorders (major depressive disorder, partial remission of major depression, minor depression, and dysthymia) in the follow up sample.

Third, we examined the subgroup of patients who had a depressive disorder at initial assessment in order to determine the proportion who were still depressed at follow up. The data on change in categorical depression diagnoses was supplemented with data on the change in total scores on the HAD scale between initial assessment and follow up.

Fourth, we determined how many new cases of depression had occurred during follow up and also calculated changes in the total HAD score of these new cases from baseline.

Fifth, in order to examine the association between change in depression status and functional status we calculated the changes in score on the SF-36 scales between the initial assessment and the eight month follow up for all patients. We then compared the changes in SF-36 scores between those patients whose depression status had changed and those whose status had remained the same.

Finally, we examined those cases who had recovered from depression in order to address the question of whether it was the change in depression or in the neurological disease that had led to changes in health status.

Comparisons were made using the statistical tests of comparison of means and the Student *t* test.

RESULTS

The results of the baseline assessment have been described in full elsewhere.[1] In summary, 300 of a possible 312 patients (96%) participated. Table 1 lists their medical diagnoses. One hundred and nineteen (40%) met the criteria for one or more DSM-IV depressive disorders (major depressive disorder, partial remission of major depression, minor depression, and dysthymia).

Of the 300 patients assessed at baseline, 226 (75%) participated in the follow up interviews. There were no deaths in the cohort during the study period. Only those patients who completed the follow up are described in the outcome data. The sample followed up comprised 88 patients (39%) who had initially had a depressive disorder (54 (24%) of whom had major depressive disorder), 17 (8%) who had an initial anxiety disorder but no depressive symptoms, and 121 (54%) who had no psychiatric diagnosis.

There was no evidence of any systematic bias by sex or depression status in the sample who participated at follow up. Although those not participating were slightly more likely to be younger and to have major depression, the difference was neither substantial nor statistically significant (table 2).

At follow up, 98 of the 226 patients (43%) were found to have a depressive disorder (major depressive disorder, partial remission of major depression, minor depression, or dysthymia). Sixty six of these patients with depressive disorders (29%) had major depressive disorder (table 3).

Of the 88/226 patients who had any depressive disorder at the baseline assessment, 69 (78%) still met DSM-IV criteria for a depressive disorder at follow up. Recovery from a depressive disorder was associated with a mean decrease of 5.5 on the HAD scale total score. Of the 54 patients who had major depressive disorder at initial assessment, 46 (85%) still had major depressive disorder at follow up. Recovery from major depressive disorder was associated with a substantial mean decrease of 10.1 on the HAD scale total score.

Of the 138/226 patients not depressed at the initial assessment, 29 (21%) had developed depression by follow up. Twenty (14%) of these patients met criteria for major depressive disorder.

Table 4 shows the comparison of mean changes in SF-36 scores between those patients who had major depression at baseline assessment but had recovered by the time of follow up and those who remained depressed. Improvements in health status associated with recovery from depression were substantial.

Table 5 shows comparisons of the mean changes in SF-36 scores in those patients who developed major depressive disorder by the time of follow up compared with those who remained emotionally well. The development of depression was associated with a substantial decline in health status.

Table 2 Comparison of baseline characteristics of the patients who participated in the follow up (n = 226) and those who did not (n = 74)

	Followed up	Not followed up	χ^2 test*	p Value
n	226	74		
Mean age (years)	43.4	39.75	–3.7 (–7.9 to 0.6)†	0.09‡
Male	93 (41%)	33 (45%)	0.3	0.7
Any depressive disorder	88 (39%)	31 (42%)	0.2	0.7
Major depressive disorder	54 (24%)	23 (31%)	1.5	0.2
Mean HAD score	11.5	11.7	0.3 (–1.8 to 2.3)†	0.8‡

Values are n (%) unless stated.
*One degree of freedom.
†Difference in means with 95% confidence intervals.
‡Student's *t* test.
HAD, hospital anxiety and depression scale.

Table 3 Psychiatric status for the whole sample at baseline and for those interviewed at the eight month follow up assessment

	Initial assessment (n=300)	Eight month follow up (n=226)
Any depressive disorder	119 (40%)	98 (43%)
depressed at initial assessment	–	69
anxiety disorder only at initial assessment	–	8
new case	–	21
Major depressive disorder	77 (26%)	66 (29%)
depressed at initial assessment	–	46
anxiety disorder only at initial assessment	–	5
new case	–	15
Mean HAD score	11.5	10.5

HAD, hospital anxiety and depression scale.

Table 4 Eight months follow up of those patients who had major depression at initial assessment showing changes in hospital anxiety and depression scale score and health status by outcome of depressive disorders (data from follow up sample, n=226)

	Major depressive disorder persists at follow up (n=46)	Major depressive disorder resolved at follow up (n=8)	Difference in means	95% CI
Mean change in HAD score	1.1	–10.1	–9.0	4.8 to 13.2
Mean change in SF36 score*				
Physical function	–4.0	13.1	17.1	5.9 to 28.4
Physical role function	–2.2	46.9	49.0	12.3 to 85.8
Bodily pain	5.3	24.1	18.8	3.8 to 33.8
Social function	5.4	26.6	21.1	–3.3 to 45.6

*All scores on the SF-36 range from 0 to 100; a lower score indicates increased disability or more pain.
CI, confidence interval; HAD, hospital anxiety and depression scale; SF-36, short form 36 item health status scale.

Table 5 Eight months follow up of patients who were not depressed at baseline showing changes in hospital anxiety and depression scale score and health status associated with the development of major depressive disorder (data from follow up sample, n = 26)

	New major depressive disorder at follow up (n=20)	Remains not depressed at follow up (n=118)	Difference in means	95% CI
Mean change in HAD score	–7.3	1.4	8.7	6.1 to 11.4
Mean change in SF-36 score				
Physical function	–14.3	0.6	15.0	7.0 to 22.9
Physical role function	–20.0	3.1	23.1	3.7 to 42.4
Bodily pain	–3.9	4.9	8.9	–3.7 to 21.4
Social function	–19.2	1.0	20.1	6.0 to 34.3

CI, confidence interval; HAD, hospital anxiety and depression scale; SF-36, SF-36, short form 36 item health status scale.

The improvements in health status following recovery from depressive illness could reflect either the recovery from depression or an improvement in the neurological condition. Unfortunately, the number of patients involved (eight) was too small to address this issue satisfactorily. However, inspection of individual case notes suggested that in the majority of cases the improvement in disability status could not be readily attributed to improvement in neurological disease.

DISCUSSION

There was a point prevalence of approximately 40% for DSM-IV depressive disorders among patients followed up eight months after their initial appointment at general neurology outpatient clinics. This was similar to the point prevalence of depressive disorders at the time of initial assessment. Over three quarters of cases of depression diagnosed at the initial assessment persisted at the eight month follow up. Twenty one per cent of those who were well at the initial assessment had depression diagnosed at follow up, indicating that neurology outpatients are at high risk of developing depressive disorders.

Recovery from major depressive disorder was associated with substantial improvement in HAD total score. Recovery from major depressive disorder was also associated with substantial improvement in overall health status. By contrast, the development of a new major depressive disorder was associated with a significant deterioration in health status. These changes in health status do not appear to be attributable to changes in neurological disease status.

There are few relevant studies with which to compare these findings. There are data from primary care settings that suggest that depressive disorders tend to persist in the absence of treatment.[8] Similar findings have been described for depressive disorders co-morbid with specific neurological diseases such as Parkinson's disease,[9] stroke,[10] and multiple

sclerosis.[11] These findings lend support to the conclusion that depressive disorders in neurological patients tend to persist.

Lesperance *et al*,[12] investigating major depression before and after myocardial infarction, reported a similar result to our own. They showed that 30 of 179 psychiatrically well patients (17%) went on to develop major depression during the six months following a myocardial infarct. We conclude therefore that patients with medical conditions of all types are at high risk of developing depressive disorders.

It has been recognised previously that depression contributes to patient disability, whether occurring on its own[13] or co-morbidly with coronary artery disease,[14 15] neurological disorders,[1] or stroke.[16] Our findings suggest that remission of major depressive disorder may also be associated with improvement in overall health and disability in patients with co-morbid neurological disease. Unfortunately, so few patients recovered that it is not possible to determine whether this improvement was explained solely by improvement in their neurological condition or whether improvement in depression also played a role. This issue is important, as depression should be amenable to effective treatment.

Our findings must, however, be interpreted in the context of methodological limitations. First, 74 patients of the original cohort, 31 of whom had depressive disorders, did not participate in the follow up assessment. It is not possible to comment on their outcome. Nonetheless, even if we assumed that they were all free of depression at follow up, the conclusion that depressive disorders persists in the majority of patients still stands. Second, as the majority of both initial and follow up assessments were conducted by a single interviewer (AC) it was not possible for the second assessment of depression to be blind to the patient's status at the initial assessment. While this is a well recognised source of bias in studies of treatment and aetiology, it is arguably less important in simple prognostic studies of this type, particularly as we had no prior expectations about the persistence of depressive disorders. Furthermore, the findings from the self report measure (HAD) were consistent with those from the interview measure (PRIME-MD). Finally, patients were not subject to a formal neurological examination at follow up, and only their case records were reviewed.

Conclusions

The majority of depressive disorders detected in a neurology outpatient setting persisted for at least eight months. Furthermore, the rate of new depressive disorders during the follow up period was substantial. Resolution of depressive disorders, particularly major depressive disorder, was associated with an improvement in health status and, although the numbers were too small for statistical analysis, it is not readily attributable to improvement in the neurological condition. There is therefore a need to establish whether interventions to treat depression would also improve health status. Such interventions may be especially important in neurological practice, where many diseases are chronic and lack specific treatments.

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REFERENCES

1 **Carson AJ**, Ringbauer B, MacKenzie L, *et al*. Neurological disease, emotional disorder and disability: they are related. A study of 300 consecutive new referrals to neurology outpatient clinics. *J Neurol Neurosurg Psychiatry* 2000;**68**:202–6.
2 **Spitzer RL**, Williams JB, Kroenke K, *et al*. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. *JAMA* 1994;**272**:1749–56.
3 **American Psychiatric Association**. Diagnostic and statistical manual of mental disorders, 4th ed. Washington DC: American Psychiatric Association, 1994.
4 **Spitzer RL**, Williams JB, Gibbon M, *et al*. (1992) The structured clinical interview for DSM-III-R (SCID). I. History, rationale, and description. *Arch Gen Psychiatry* 1992;**49**:624–9.
5 **Zigmond AS**, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–70.
6 **Ware JE**, Snow KK, Kosinski M, *et al*. *SF-36 health survey manual and interpretation guide*. Boston: The Health Institute, 1993.
7 **Wells KB**, Burnam MA, Leake B, *et al*. Agreement between face-to-face and telephone administered versions of the NIMH diagnostic interview schedule. *J Psychiatr Res* 1988;**22**:207–20.
8 **Zung WWK**, Magruder-Habib K, Velez R, *et al*. (1990). The comorbidity of anxiety and depression in general medical patients. *J Clin Psychiatry* 1990;**51**(suppl):77–80.
9 **Brown RG**, MacCarthy B, Gotham AM, *et al*. (1988) Depression and disability in Parkinson's disease: a follow up of 132 cases. *Psychol Med* 1988;**18**:49–55.
10 **Astrom M**, Adolfson R, Asplund K. Major depression in stroke patients: a three year longitudinal study. *Stroke* 1993;**24**:976–82.
11 **Ron M**, Feinstein A. Multiple sclerosis and the mind. *J Neurol Neurosurg Psychiatry* 1992;**55**:1–3.
12 **Lesperance F**, Frasure Smith N, Talajic M. Major depression before and after myocardial infarction; its nature and consequences. *Psychosom Med* 1996;**58**:99–110.
13 **Wells KB**, Stewart A, Hays RD, *et al*. The functioning and well-being of depressed patients. Results from the medical outcomes study. *JAMA* 1989;**262**:914–19.
14 **Frasure-Smith N**, Lesperance F, Talajic M. Depression and 18-month prognosis after myocardial infarction. *Circulation* 1995;**91**:999–1005.
15 **Sullivan MD**, LaCroix AZ, Baum C, *et al*. Functional status in coronary artery disease: a one–year prospective study of the role of anxiety and depression. *Am J Med* 1997;**103**:348–56.
16 **Parikh RM**, Robinson RG, Lipsey JR, *et al*. The impact of post stroke depression on recovery in activities of daily living over a 2-year follow-up. *Arch Neurol* 1990;**47**:785–9.