Regular Review

Depression after stroke

ALLAN HOUSE

Stroke has an annual incidence in Britain of about 200 cases for every 100 000 population and a prevalence of about 500 for every 100 000.[1] Survivors may return to an entirely normal life, but about a third do not achieve functional independence.[2] Mood disorder may be a specific complication of stroke,[3] and failure to recognise and treat the disorder may be an important unmet need of survivors of stroke.[4]

Difficulties in measuring and diagnosing depression in survivors of stroke

"Depression" is used rather loosely to cover a range of unpleasant mood states. After a serious illness a patient may experience an adjustment reaction, which usually arises early and is akin to normal grief, or major depression, which tends to develop later, is associated with more persistent biological symptoms, and may respond best to physical methods of treatment. Unfortunately, claims about the frequency and importance of depression after stroke have not always been based on adequate accounts of what is meant by depression. Claims that the depression goes untreated are thus difficult to assess,[4 5] particularly because the symptom profile rather than simply the symptom level provides the best indication for antidepressants.[6]

Another difficulty is that brain damage may be associated with mood changes that are not well described by the standard psychiatric nomenclatures. Some patients are abnormally indifferent or apathetic, while others show only intermittent disturbance. For instance, in the "catastrophic reaction" described by Goldstein anxiety, tears, or aggression are not persistent but appear only when a patient is provoked by the request to perform a task beyond his or her capacity—in other words, the cardinal feature is not "catastrophe" but "reaction."[7] Irritability is another well recognised symptom of brain damage that is rarely formally assessed.[8] Pathological emotionalism—that is, "forced" or inappropriate crying (and very rarely laughing)—is usually thought of as organically based[9] but may be associated with a depressive illness and occassionally responds to antidepressants.[10]

What then is the best way to make a diagnosis? Several studies have used global judgments made by a research nurse,[11 12] patients, or carers.[4 13] This approach conforms closely to routine clinical practice, but the vegetative symptoms of depression (such as anorexia, insomnia, and retardation) are similar to the physical sequelae of stroke; these informal judgments may not therefore provide a reliable guide to clinically important depression.

In an effort to improve reliability self report inventories have often been used. Such inventories have been validated in several medical settings but tend to have relatively low specificities and predictive values because including somatic symptoms leads to high false positive rates.[14] The general health questionnaire (GHQ 28), Zung depression scale, and Wakefield depression inventory have all been used, but none has been validated against standard clinical criteria for depression in survivors of strokes, although scores on these scales correlated well with each other in one study.[15] Even the normal elderly may require higher cut off scores than those used for younger adults.[16]

Another important problem is that survivors of strokes may not be able to complete the forms. This is true of up to one third of patients immediately after stroke.[5 17] Many of those who do complete the form have had the questions read to them, which introduces further doubts about the use of cut off scores derived from patients without brain damage who have completed the form unaided. The influence of the interviewer on the answers may also be important. Setting a higher threshold on the Wakefield inventory in one study[9] was thus understandable, but it illustrates the arbitrary nature of many decisions in these studies.

Another way to make a psychiatric diagnosis is to use a standardised interview—usually either the Hamilton rating scale[18] or the present state examination.[19] The Hamilton scale is heavily loaded with somatic questions, and the present state examination therefore seems best. Robinson *et al* modified both the scoring and the questions of the present state examination, emphasising behavioural ratings.[15 17] Their results cannot therefore be directly compared with those of other studies based on this examination. Other forms of mood disorder such as pathological emotionalism cannot be easily rated on the present state examination or any other instrument, and no attempts have been made to describe their occurrence systematically.

The absence of an entirely satisfactory clinical diagnostic procedure has led to the search for a laboratory test for depression. A recent favourite has been the dexamethasone suppression test, but it is not sensitive or specific enough to be useful as a routine clinical test for depression.[20] A careful clinical interview therefore remains the mainstay of diagnosing mood disorder after stroke.

Rates of depression after stroke

The failure to use uniform measures for depression makes comparison of figures from different studies impossible. In the discussion below the term "depression" sometimes refers to a single symptom, sometimes to a state defined by a score

on a rating scale that may not have been validated in patients with stroke, and sometimes to one of several clinically diagnosable mood disorders with specific symptoms.

Rates of depression of 27%[17] and 22%[5] have been reported in the first weeks after stroke, and the prevalence falls only slightly over the next six months[4 11 15 17] or one to two years.[5 21] Some long term survivors may, however, have lower rates of depression.[15] None of these studies considered whether the depression started before rather than after the stroke. Depression is found in about 15% of the elderly at home,[22-24] and so depression may be almost twice as common among patients in the first year after stroke as among the normal elderly population.

Depression is commoner among the elderly who have recently been ill or who have chronic health difficulties,[23] and the question therefore arises whether depression is more common after stroke than after other physical illnesses. Two small studies comparing patients who had had strokes with other disabled patients came to opposite conclusions.[3 25] A further study showed depression to be commoner among patients who had had strokes than among those who had had myocardial infarctions, but irritability and emotional instability were equally common in both groups.[26] The prevalence of depression after a stroke is similar to that found after many medical illnesses, although symptoms rarely persist more than a few months after the onset of most other physical illnesses.

All the studies I have quoted may be criticised for their choice of study population: only five reports are based on over 50 patients; one described patients attending an outpatient clinic,[15] three described consecutive hospital admissions,[11 17 21] and only one was based on a community sample.[5] Many patients are not admitted to hospital after strokes (more than half in some areas[27]), and many of the patients in these studies have a history of stroke and are socially disadvantaged. Attrition in the sample is another problem; for example, Robinson *et al* saw only 61 of their original 103 patients within six months of their stroke.[28] Another potential source of selection bias is that patients with dysphasia or confusion are often excluded.

Thus it is unproved that depression is commoner in an unselected group of patients after strokes than it is among the elderly with other physical illnesses.

Aetiology of depression after stroke

Stroke may be interpreted by the elderly as a loss or a threat.[29] It may well lead to long term physical disability and impaired social functioning,[2 30] and depression is associated with this impaired social functioning.[6 21 30] The patients' relationships may be strained by chronic behavioural problems, sexual difficulties,[31] or dysphasia, and psychopathology is common among carers.[32]

The attitude of others may make it harder for patients to come to terms with their difficulties. Doctors in hospitals rarely approach patients who have had strokes with sustained interest, and dignity and status may be lost with the misplaced hearing aid, spectacles, or dentures. Once a patient goes home friends may give up the calls they made regularly when he was "ill" in hospital. When the general practitioner says "Call me if you have any problems" it is often interpreted as "Don't call me unless you have any new problems"—and the patient is left regretting the lack of a visit from a potential source of much support.

Brain lesions of all sorts often have psychiatric sequelae.[33 34] Lishman considered that three quarters of his patients who had had head injuries and who were the most psychiatrically disturbed had predominantly affective symptoms, and some 15-20% of patients with cerebral tumours have depression.[33] The size of the lesion correlates only slightly with depression, which may occur after minor cerebral trauma.[35] Intellectual impairment and depression are associated, but only weakly.[36] Some of this correlation may be caused by depression itself leading to reversible intellectual impairment in patients who have had strokes.[37] An indirect measure of brain damage is subsequent physical disability, and again depression is associated only weakly with standard measures of this.[5]

Might depression after stroke be more closely related to the site of damage? Much recent interest has focused on the role of localised and particularly lateralised hemisphere damage in psychological disorders,[38-40] and Robinson and others have pressed the case for depression after stroke being caused particularly by lesions in the anterior left hemisphere.[12 41] Depression is said to be common in aphasic patients[42 43] but has also been claimed to be common in those with left hemisphere damage who are right hemisphere dominant.[44] Damage to the right hemisphere is associated with neglect and inattention to a range of stimuli and may lead to apathy or indifference that extends to personal and social matters.[7 45-47] There is also considerable experimental evidence that damage to the right hemisphere is associated with disturbed processing of emotionally important material.[48-51]

The case for depression after stroke being associated with lesions in the left hemisphere is, however, far from proved. Intracarotid amylobarbitone has produced conflicting results on the emotional responses of the two hemispheres,[52] and many of the observations on brain damaged subjects are based on neuropsychological testing rather than on clinical symptoms. Some clinical studies have suggested that right hemisphere damage may be positively associated with serious mood disorder,[53] or that mood disorder is unrelated to the side of the lesion.[5 15 54] In Gainotti's much quoted study catastrophic reactions were commoner in patients with left hemisphere damage and indifference reactions in those with right hemisphere damage, but there were no differences between the two groups on measures of depression.[7] Deficits considered "typical" of right hemisphere damage—such as neglect or disturbed affective prosody (emotional intonation and rhythm)—are found after lesions in other parts of the brain.[55 56] Depression is also associated with neurological disorders where the lesion is mainly subcortical—for instance, Parkinson's disease.[57]

Thus the degree of brain damage is only weakly associated with subsequent emotional problems, and there is no conclusive proof that damage in any specific site is particularly likely to lead to depression. Depression after stroke is probably largely determined by social factors.

Treatment of depression after stroke

Depression after stroke may lead to increased social and functional disability[30 36] and perhaps even to failure to leave hospital.[58] The mood disorder has usually been thought of as a consequence of the patient's difficulties and therefore as being best managed by an active rehabilitation programme combined with reassurance, advice, and education for both patient and family.[29 59 60] Such counselling should cover the patient's fears about becoming dependent and about the stroke recurring.

Little attention has been given to physical methods of treatment. Although they are often prescribed in hospital,[61] drugs do not tend to be used in general practice for patients who are depressed after strokes.[5] Care needs to be taken in prescribing antidepressants because blood concentrations may be unpredictable in the elderly.[62] The drugs may cause sedation, confusion, or epilepsy in those with cerebral injury. In the only reported randomised trial of treating depression after stroke with a tricyclic antidepressant (nortriptyline) blood concentrations were monitored, but even so six out of 17 patients having active treatment did not complete the study because of side effects.[63] In those who did complete the trial nortriptyline improved all measures of depression, and the authors concluded that the drug "represents a potentially important advance in the treatment of stroke patients." A more cautious interpretation might have been better because of the small and selected sample and the high drop out rate because of drug side effects.

Despite the lack of formal evidence, most doctors find physical methods of treatment of great help in individual cases. A tricyclic antidepressant such as dothiepin or amitriptyline may be introduced at low dosage (25-50 mg daily) and the dose gradually increased to the maximum tolerated (probably about 100-150 mg daily). The main indications are (*a*) biological or psychotic symptoms of depression; (*b*) persistent depressed mood, even without biological symptoms, which does not respond to counselling or to changes in social setting such as day care; and (*c*) atypical depressive presentations such as hypochondriasis or pseudodementia. Stroke is not a contraindication to electroconvulsive therapy,[64] which can be used for major depression unresponsive to antidepressants and in patients who have biological or psychotic features or a high risk of suicide. Electroconvulsive therapy is usually not used within three months of stroke, but otherwise there are no special contraindications.

Conclusions

The ideal study of depression after stroke would be community based with minimal exclusions; use clinical judgments based on standardised interviews and operational criteria for assessing dysphasia, pathological emotionalism, indifference, and confusion; and describe the results in terms of a widely used system of diagnostic classification. No such study has been done, and until it has been the claim that depression after stroke is underdiagnosed and undertreated by physical methods cannot be accepted.

Pending further research, doctors should regard depression after stroke as they would depression after other physical illnesses. Most important is discussion with patient and family and provision of services aimed at social and physical rehabilitation. For the minority in whom symptoms persist then a proper trial of a tricyclic antidepressant is a reasonable strategy. The patient should be referred to a psychiatrist in cases of diagnostic uncertainty, expected problems with treatment, and the failure of first line management.

ALLAN HOUSE

MRC Research Officer,
Oxfordshire Community Stroke Project,
Radcliffe Infirmary, Oxford OX2 6HE

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