Depression and its relation to lesion location after stroke

Siobhan M MacHale, Suzanne J O'Rourke, Joanna M Wardlaw, Martin S Dennis

Abstract
The study of discrete organic cerebral lesions resulting in clearly definable psychiatric disorders may provide an understanding of the underlying pathophysiological basis of these disorders. However, the relation between lesion location and psychiatric illness after stroke remains unclear. Fifty five patients referred to hospital were identified who had a single lesion on CT which was consistent with their neurological presentation and who did not have evidence of a persistent affective disorder at the time of the stroke. Six months after stroke standardised psychiatric assessment disclosed that 26% of the patients met DSM-IV criteria for an anxiety or depressive disorder, with depression the most common diagnosis (20%). Pathological emotionalism was diagnosed in 18% of patients, particularly those who were depressed (p<0.0001). Depression was significantly associated with larger lesions involving the right cerebral hemisphere (p=0.01). The importance of depression as a consequence of stroke has been clarified by the studies in this area. However, wide confidence intervals support the possibility that significant results may be due to chance. A systematic review of these studies is now needed if a consensus is to be reached.

Patients and methods
One hundred and eighty seven patients referred to a city hospital with a clinical diagnosis of stroke were consecutively identified as part of a randomised trial of a stroke family care worker. Criteria for inclusion into the randomised trial were inpatient or outpatient assessment at the hospital within one month of having a stroke, residence within 25 miles, consent to follow up, and likelihood of survival. Of these, 16 (9%) patients died in the first six months and seven (4%) refused follow up. A further 19 (10%) patients were excluded because of severe cognitive deficits (15 patients with a mental test score <5) or severe aphasia (four patients) which precluded psychiatric interview. Fourteen of these 19 patients had left hemispheric lesions on CT.

Six months after randomisation, 145 (85%) survivors had a psychiatric assessment carried out at their place of residence. The schedule for affective disorders and schizophrenia (SADS), a standardised semi-structured psychiatric interview, was used to generate a DSM-IV psychiatric diagnosis. Diagnoses were grouped as either depressive disorders (comprised of major depressive disorder, depressive disorder not otherwise specified, or adjustment disorder with depressed mood) or anxiety disorders (comprised of generalised anxiety disorder, agoraphobia with or without panic disorder, simple phobia or adjustment disorder with anxious mood) for the purposes of analysis. The short emotionalism questionnaire was administered to allow diagnosis of pathological emotionalism as defined in the Oxfordshire Community Stroke Project—that is, an increase in tearfulness with episodes of crying or laughter that were sudden or unheralded and not all under normal social control. An observer rated measure of ability to perform 10 basic activities of daily living such as dressing and eating was used to assess physical disability (Barthel index).

Keywords: depression; stroke

Over the past decade there has been an upsurge of interest in research into neuropsychiatric disorders after stroke. This has paralleled the expansion of biological psychiatry, based on the assumption that knowledge of discrete organic brain lesions resulting in clearly definable psychiatric illnesses will provide an understanding of the underlying pathophysiological basis of these disorders.

Both stroke and affective illnesses are common, but how often they coexist remains unclear. Reported rates of depression after stroke have ranged from 14 to 60% depending on factors such as populations sampled, time of assessment after stroke, and diagnostic instruments used. Equally unclear is the relation between lesion location and psychiatric illness. With studies reporting an association between depression and left anterior lesions, right hemispheric lesions, or no association with right or left cerebral pathology, the debate continues.

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Received 1 May 1997 and in revised form 26 August 1997
Accepted 28 August 1997
hospital anxiety and depression scale (HADS)\textsuperscript{18} to complete and return by post.

Of the 145 patients, 131 (90%) had brain CT within six weeks of their index stroke. All scans were done on an IGE 8800 CT scanner with fast upgrade, using standard 10 axial slices through the whole brain at 1 cm intervals. Scans were read blind to all clinical findings by a consultant neuroradiologist (JW) and all visible stroke lesions (infarct or haemorrhage) were classified according to site, volume, and whether cortical or subcortical (depth), recent, or old. No tumours were identified. An infarct was defined as an area of low density (relative to normal brain) which occupied a vascular territory and might be swollen, atrophied, or haemorrhagic depending on its age. A haemorrhage was defined as an area of increased density, usually rounded, with mass effect. Lesion site was identified according to the hemisphere involved and anterior or posterior position according to the topographical criteria employed by Starkstein \textit{et al.}\textsuperscript{19} Hence, the anterior location of the lesion was defined as the mean distance of the anterior border of the infarct from the frontal pole averaged over all slices in which it was visible. This measurement was then expressed as a percentage of the greatest distance between the anterior and posterior poles of the brain (A-P distance). Lesions were described as “anterior” if their anterior border was less than 40% of the A-P distance. “Posterior” lesions were defined as those in which the anterior border was posterior to 40% of the A-P distance. Lesions were subdivided into cortical or subcortical depending on depth. Volume was estimated according to the method of Pullicino \textit{et al.}\textsuperscript{20} Each of the methods described has been employed in previous studies of psychiatric morbidity after stroke.\textsuperscript{3, 21}

Non-parametric tests of significance were used as most of the measures were not normally distributed. Fisher’s exact probability test was used in tests of dichotomous variables when small numbers were involved. The Mann-Whitney \textit{U} test allowed comparisons between groups of continuous data. Two tailed tests of probability were chosen along with a minimum significance level of \(p<0.05\). Forward stepwise regression analysis was used to test the strength of association between depression and potentially confounding variables.

\textbf{Results}

All 145 patients were white, with a mean age of 66 (range 18–93), and a slight excess of men (52%). Most were married or widowed (81%) and living in their family home (96%). Three quarters (109) of the patients had never had a previous stroke and 114 (79%) required admission to hospital. Over half the patients had no residual neurological disability six months after the stroke, with the remainder either mildly (Barthel index score 15–19) disabled (33%), or moderately to severely (Barthel score <15) disabled (15%).

Thirty eight patients (26%) met DSM-IV criteria for an anxiety or depressive disorder. Depressive illness was the most common psychiatric diagnosis, affecting 29 patients (20%). Younger patients (\(U=1201, p=0.03\)) and those with greater physical disability (\(U=954, p=0.001\)) were significantly more likely to be depressed. Pathological emotionalism was diagnosed in 26 (18%) patients. Emotionalism was significantly associated with depression (\(p=0.0001\)), with 16 (62%) of these patients also meeting criteria for a depressive illness. Complete data were available for the HADS in 105 (72%) patients, with most non-completions due to either an inability to comprehend questions or failure to return the self report questionnaire. With a cut off score of 8/9, 21 patients were diagnosed as depressed on the HADS compared with 18 with the SADS, and seven had a diagnosis of anxiety (without comorbid depression) on both HADS and SADS assessment.

Of the 131 patients who had CT, 46 had no lesion visualised. On 15 scans the lesion identified was incompatible with the neurological deficits on clinical assessment. A further 10 scans were excluded because of either multiple or cerebellar lesions. Finally, five of the remaining 60 patients had a retrospective diagnosis made of an anxiety or depressive disorder at the time of their stroke and so were also excluded. The relation between psychiatric diagnoses and lesion location was then analysed in the 55 patients who had a single lesion location of psychiatric morbidity after stroke.\textsuperscript{32} 1

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<th>Right hemisphere</th>
<th>Left hemisphere</th>
<th>Anterior (n=22)</th>
<th>Posterior (n=33)</th>
<th>Right anterior (n=11)</th>
<th>Other (n=44)</th>
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\textit{Note:} Significant comparisons were made using \textit{p}=0.05.
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with severe comprehension deficits.\textsuperscript{23} location and, as yet, there remains no reliable but the two may coexist, depending on lesion lesions. Starkstein and Robinson have sug-

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85% of patients who survived to six months overall with respect to a diagnosis of depres-

hadeithernoormildneurologicaldisabilityis
depression six months after stroke.\textsuperscript{92 2} 

different between anterior and posterior lesions
to an underestimate of psychiatric morbid-

In this study we report an association between

depression and a diagnosis of emotionalism.

Firstly, the period of time which has elapsed

Discussion

This study is supportive of Lishman’s\textsuperscript{18}

report of an association between affective

disorders and both right hemispheric and fron-
tal lobe damage after penetrating brain

hemispheric lesions, particularly those in-

volving the anterior region, and depressive

illness six months after stroke. Our finding that

85% of patients who survived to six months had either no or mild neurological disability is comparable with community based reports.\textsuperscript{8 22} 

The exclusion of a number of patients in this, as in other studies,\textsuperscript{8 11 21} because of severe cogni-
tive or communicative deficits may contrib-

ute to an underestimate of psychiatric morbid-

ity in those patients with left hemispheric

lesions. Starkstein and Robinson have sug-
gested that aphasia does not cause depression,

but the two may coexist, depending on lesion

location and, as yet, there remains no reliable

method of assessing mood disorders in patients

with severe comprehension deficits.\textsuperscript{23}

There are reasons contributing to the lack of consensus on a possible association between lesion location and depression after stroke. Firstly, the period of time which has elapsed after the stroke is an influential factor in the association between location of lesion and depression. Much of the work of Robinson and colleagues involved assessing patients within the first few weeks after stroke, although, they also confirmed the importance of left anterior pathology in depression six months and one year after stroke.\textsuperscript{24} A study which specifically considered this question reported that left anterior lesions only predicted major depres-
sion in the acute stage after stroke, but not at three or 12 months.\textsuperscript{3}

Secondly, studies emphasising the relevance of left anterior pathology have considered more disabled inpatient populations,\textsuperscript{1,5} with neither of two recent community based studies finding a significant association between location of lesion and depression after stroke.\textsuperscript{11} The study of Dam et al of a similar group of patients as ours (inpatients or outpatients at the hospital neurological department) have reported a significantly higher degree of depression in patients with right hemispheric lesions, with the highest degree of symptoms found in those with right anterior pathology.\textsuperscript{6}

Finally, Ross and Rush have cautioned clini-
cians about the flattened affect and aprosodic speech which may accompany right sided lesions, causing statements of low mood “delivered in an unconvincing, flat monotone devoid of affective qualities” to be disregarded.\textsuperscript{25} They have also emphasised the critical role of denial of emotional or neurological impairment in patients who have sustained a right hemispheric injury. The Rob-
inson group’s initial work required a patient’s admission to feeling sad or depressed before diagnosing a depressive illness\textsuperscript{26} but later reported that depression was equally frequent among patients with or without anosagnosia.\textsuperscript{37}

This study is supportive of Lishman’s\textsuperscript{18}

of emotion that is restricted.”

The importance of depression as a conse-
quence of stroke has been clarified by the stud-
ies in this area. However, due to the small numbers involved in individual studies incor-
porating heterogeneous patient populations, the role of lesion location remains unclear. Wide confidence intervals support the possibility that significant results may be due to chance. A systematic review of these studies is now needed if a consensus is to be reached.

We thank Dr Douglas Blackwood as the M Phil supervisor of the first author (SM), from which this thesis paper developed.
14 Endicott J, Spitzer R. A diagnostic interview. The schedule for affective disorders and schizophrenia. Arch Gen Psychiatry 1978;35:837–44.