Original Paper

Cerebrovascular Diseases

Cerebrovasc Dis 1996;6:208–215

The Place of Site of Lesion in the Aetiology of Post-Stroke Depression

P.W. Burvill
G.A. Johnson
T.M.H. Chakera
E.G. Stewart-Wynne
C.S. Anderson
K.D. Jamrozik

Department of Psychiatry and Behavioural Science, University of Western Australia, and Department of Neurology, Royal Perth Hospital, Perth, Australia

Key Words
Depression
Stroke
Lesion location
Aetiology

Abstract
The association of post-stroke depression (PSD) and site of cerebral lesion was investigated in 117 patients with first-ever stroke in the Perth Community Stroke Study, who were depressed 4 months post-stroke. The site of lesion was previously localised by studying the CT scan in conjunction with the atlas of neuroanatomy and cranial computed tomography of Kretschmann and Wainrich, rather than the topographical approach used in most previous studies. Patients who were depressed immediately prior to the stroke were excluded. No support was found for the assertion that lesion location is a prime factor in the aetiology of PSD. Future investigations of this topic should encompass a much broader range of variables than lesion location, as the aetiology of PSD is likely to be multi-factorial.

The most influential and prolific investigators of post-stroke depression (PSD) have been Robinson and his co-workers, who have advocated the view that the location of the lesion in the brain is the most important factor determining whether or not the patient with a stroke becomes depressed [1–6]. They have reported the following findings: There is a significantly increased frequency of both major and minor depression associated with (i) left, rather than right, hemisphere lesions; (ii) left anterior cortical lesions rather than left posterior cortical lesions; (iii) left anterior lesions rather than right anterior lesions; (iv) left anterior brain lesions compared with any other lesion location in the brain: (v) cortical or sub-cortical lesions involving at least part of the left dorso-lateral frontal cortex rather than the left posterior cortical or right cortical areas, and (vi) right ganglia lesions. Furthermore, they have stated that patients with major depression and concomitant anxiety were significantly more likely to have left cortical lesions than patients with major depression without anxiety symptoms, who were more likely to have left sub-cortical (basal ganglia) lesions. Patients whose depression spontaneously remitted within six months had a significantly higher frequency of sub-cortical or brainstem lesions, compared with those without early remission, who had cortical lesions. However these findings of Robinson's group have come from studies on predominantly middle-aged, black, inner-city-dwelling patients and may not be applicable to other stroke populations [7].

The original hypothesis of Robinson [8] for the importance of left anterior lesions in the aetiology of depression following stroke derived from laboratory experiments on

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1015–9770/96/0064–0208$10.00/0

P.W. Burvill
Department of Psychiatry and Behavioural Science
University of Western Australia
Nedlands, W.A. 6009 (Australia)

Received:
April 26, 1995
Accepted:
October 10, 1995

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rats which showed that focal cortical lesions produced widespread but asymmetrical depletion of catecholamine concentrations depending upon which hemisphere is injured. Thus, it was postulated that anterior lesions in human would damage areas with high concentrations of biogenic amine pathways and put the patient at greater risk for depression. A detailed explanation of this hypothesis has been provided by Starkstein et al. [9].

Three recent studies from other investigators [10–12] have added some confirmation for the proposed relationship between PSD and lesions located in the left anterior hemisphere [13] although a fourth [7] did so only after patients depressed pre-stroke were excluded. The numbers of patients involved in three of these studies were small. There are also a number of studies that have failed to confirm the relationship and four recent reviews of the literature acknowledge that the data reported so far do not allow firm conclusions to be drawn about characteristics of cerebral lesions [14–17]. The most trenchant criticism of the association between location of the lesion and PSD has come from the Oxfordshire Community Stroke Project (OCSP) Group [14, 18] who believe that depression after stroke is probably largely determined by social factors. An important theme emerging from the recent literature on PSD has concerned other risk factors for depression, e.g. age, gender, personality development, neuroticism, degree of disability, lack of social support, dependence on others for activities of daily living, negative life events, and both personal and family history of affective disorders and anxiety [13]. Morris et al. [7] have suggested that, although location of the lesion may be an aetiological factor in some PSD, other variables that increase vulnerability to depression should be controlled for in future studies on this topic.

Three major methods of measuring the incidence of PSD have been used by various investigators. Early studies used questionnaires such as the Beck Depressive Inventory. Most investigators have adopted the method used by Robinson's group, namely a structured psychiatric interview schedule which enabled a DSM-III or DSM-III-R diagnosis to be made, and categorised depression as either major depression (DSM-III) or minor depression. Cases of the latter were those who satisfied the DSM-III criteria for dysthymia, but without the 2-year duration requirement [4]. The OCSP used the Present State Examination (PSE) [19] and the PSE-ID-CATEGO system [20] to derive a diagnosis of depression. They found that the scores for PSD using the Beck Depressive Inventory and the PSE 1 month after stroke were continuously distributed [21]. Thus, it is quite likely that the major and minor depression categories used by Robinson's group are two ends of a unidimensional spectrum of depression. In fact, many investigators have combined major and minor depression to form 'depressive disorders'.

Almost all studies to date have adopted the topographical approach to localisation of the cerebral lesion described by Starkstein et al. [2] which measures the distance of the lesion from the frontal pole and/or inclusion of the lesion within arbitrarily defined sections of the anterior-posterior distance on CT scan. This method of localisation has been criticised by House [21] and Johnson [17] as it does not conform very closely to neuro-anatomical boundaries and does not satisfactorily separate cortical from sub-cortical lesions. It is not a method that has much relevance or meaning to neurologists and neuro-radiologists.

In 1989–1990, a community-based study of stroke was conducted in Perth, Western Australia, by a multi-disciplinary team – the Perth Community Stroke Study (PCSS). The method employed for this study and preliminary findings have been described by Anderson et al. [22, 23], and the prevalence of post-stroke depression and of anxiety by Burvill et al. [24, 25]. The aim of this paper is to examine the relationship between the site of the cerebrovascular lesion and depressive illness 4 months post-stroke, using conventional neurological/radiological methods of localisation of the cerebral lesion, in patients with a first-ever stroke from the PCSS who were not depressed at the time of the stroke. The specific aims were to test the two null hypotheses that there is no difference in the prevalence of PSD between patients with lesions (i) in the left versus the right cerebral hemispheres, and (ii) in any particular neuro-anatomically defined area within each hemisphere. The study employed the same method to diagnose and classify depressive illness as that used by Starkstein and Robinson [4], but followed the more traditional method of locating lesions according to neuro-anatomical landmarks.

Patients and Methods

The Perth Community Stroke Study (PCSS)

Details of case ascertainment and baseline assessment of patients seen in the PCSS have been described in full by Anderson et al. [22]. Briefly, all residents of a geographically defined segment of the Perth metropolitan area (estimated population 69,008 males and 69,700 females at June 30th 1989) who had a stroke between 20th February 1989 and 19th August 1990 were included in the PCSS. A variety of overlapping sources of case ascertainment was used. These included notifications from general practitioners; scrutiny of all attendances at and admissions to all acute hospitals, rehabilitation centres and nurs-

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ing homes; coroners' reports and death registrations; and surveillance of computerised hospital discharge statistics. All patients were seen as soon as possible after an event by the study registrar (CSA) who conducted a standardised interview and physical examination, and confirmed that they had had a stroke. Stroke was defined according to WHO criteria [26] and the new special report from the Institute of Neurological Disorders and Stroke [27]. 492 patients were detected of whom 408 were interviewed by CSA. 69% had had a first-ever stroke. 83 patients had died before being seen by the registrar and only 1 patient refused to take part in the study. Twenty percent of all stroke events were managed entirely outside hospital, either at home or in a nursing home. None of the patients had further strokes within four months after onset.

Radiological Assessments

If he or she had not already done so, the doctor in charge of the case was asked to consider having a cranial CT scan or magnetic resonance imaging (MRI) performed on the patient. Only 19 patients had MRI. Ideally, a patient had a CT scan performed within 14 days of a stroke but intravenous contrast was not routinely given because of the potential risk of adverse reactions. In selected cases, additional CT scans, or both CT and MRI were performed on the same patient, but this was not specifically requested as part of the study. Patients seen 30 days or more after their stroke generally had MRI because of the greater sensitivity over CT in detecting cerebrovascular lesions [28]. The location of the lesion was described according to the neuroanatomical areas listed in table 1, using the atlas of Kretschmann and Weinrich [29]. New lesions were differentiated from old lesions resulting from previous strokes. The classes of lesion location used in table 3 were made up of the following areas [table 1): fronto-temporal: frontal, insular/opercula, and temporal; parieto-occipital: parietal and occipital; deep white matter: internal capsule, corona radiata and boundary zone; deep nuclei: caudate, putamen, globus pallidus and thalamus; posterior fossa: cerebellum and other.

Psychiatric Assessment at Four Months

The patients with stroke were seen at 4 months after the index event. 319 patients from the original cohort were still alive, but 7 of these had moved out of Western Australia. The remaining 312 patients were physically assessed by CSA, and 248 of them were seen for psychiatric assessment by either P.W.B. or G.A.J. Four patients died shortly after assessment by CSA, before being seen by one of the psychiatrists, and 13 refused to see a psychiatrist. Forty-three patients were too severely demented and 3 too severely aphasic to enable a full psychiatric assessment to be made, including an assessment of their mood. The 43 severely demented patients were unable to engage in a meaningful conversation and to answer questions necessary for such an assessment. These patients were not included in the study reported in this paper. In calculating the prevalence of depression a denominator of 294 patients at risk was used, this being composed of the 248 (84%) seen by the psychiatrists, the 43 (15%) patients with severe dementia, and the 3 (1%) with severe aphasia [24].

Patients were seen in their own homes, in nursing homes, or occasionally in the psychiatrist's office. Each patient was assessed using the Psychiatric Assessment Schedule (PAS) [30], which is a modified version of the Present State Examination (PSE) [19], and which enables diagnoses of depressive and anxiety disorders to be made according to both DSM-III and PSE criteria. Careful enquiry was made by the psychiatrists of each patient and of relatives where available, as to the presence or absence of any psychiatric disorder, especially of depression or anxiety disorder, at the time of the index stroke. Depression and emotional lability were clearly distinguished as the latter can be a complication of stroke [14]. The psychiatrists were blind to results of the CT scans.

Analysis

All data were collected on pre-coded interview forms and entered onto a database held in a mini-computer system. The data were ana-

Table 1. Distribution of stroke lesions on CT scan and association with post-stroke

	Left				Right			
	lesions	major depr.	minor depr.	total depr.	lesions	major depr.	minor depr.	total depr.
Frontal	4	0	2	2	5	0	2	2
Parietal	3	0	0	0	4	1	1	2
Insular/opercula	4	0	0	0	2	1	1	2
Occipital	5	1	1	2	4	0	1	1
Temporal	12	4	1	5	13	3	1	4
Caudate/putamen/globus pallidus	5	2	1	3	3	2	0	2
Thalamus	1	0	0	0	2	0	0	
Internal capsule	6	0	0	0	4	1	0	1
Corona radiata	15	1	1	2	15	3	0	3
Boundary zone	2	1	0	1	1	0	0	0
Cerebellum	5	0	2	2	7	2	0	2
Other	1	0	0	0	1	0	0	0
Total	63	9	8	17	61	13	6	19

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lysed using the SAS [31] and EGRET [32] statistical packages. A non-hierarchical approach to diagnosis was used with the PAS data so that each patient was assigned all the DSM-III diagnoses for which he or she satisfied the criteria. Depressive disorders were categorised as either major depression (DSM-III) or minor depression. In accordance with the criteria adopted by Robinson and his colleagues in their studies of post-stroke depression in Baltimore, cases of minor depression were those who satisfied the DSM-III diagnostic criteria for dysthymia, but not the requirements for a duration of two years [4]. All patients who were (i) assessed by a psychiatrist at 4 months; (ii) had a lesion visible on CT scan or MRI, (iii) had a first-ever stroke, and (iv) were not depressed at the time of the stroke, were included in the present study. Owing to the small numbers involved, the Fischer Exact Probability Test, rather than the χ^2 test, was used to test differences in the prevalence of major or minor depression at 4 months post-stroke in groups of patients defined by the locations of their cerebrovascular lesion, as listed in table 1. In addition, in all tests of statistical probability an odds ratio was calculated.

Results

In the PCSS, of the 221 patients who had first-ever strokes, 33 (15%) had a major depression and 21 (9%) minor depression, giving a total of 54 (24%) with some type of depressive illness at 4 months post-stroke. Of these 221 patients 117 who were not depressed at the time of the stroke had lesions on cerebral CT that were compatible with clinical features of the stroke. All the results reported in this paper are based on these 117 patients.

Table 1 outlines the distribution of all the lesions by neuroanatomical site and by the presence of either major or minor depression. Lesions were evenly distributed between the left and right hemispheres. There are a total of 124 lesions listed as, in 7 patients (3L, 4R), the lesions occupied more than one of the listed neuroanatomical sites. Of the 117 patients 20 (17%) had major depression and 13 (11%) minor depression, giving a total of 33 (28%) of patients with a depressive illness.

Side of Lesion

A higher percentage of patients with lesions in the right (21%) than in the left cerebral hemisphere (13%) had major depression, but these differences were not statistically significant (table 2). the proportion with minor depression was very similar in those with left (12%) and right (11%) hemisphere lesions.

Detailed Lesion Location

Table 3 outlines a classification of lesion location which is meaningful from the viewpoint of neurologists experienced in dealing with patients with stroke. This classification is an amalgamation of the more detailed neuroanatomical sites listed in table 1, as detailed in the 'Methods' section. There was a very similar distribution of lesions, and of the proportion with depression within each site, between the left and right hemispheres of the brain. None of the differences between the left and right sides was statistically significant.

The hypotheses, frequently asserted in the literature, that there is a significantly increased frequency of depression associated with (i) anterior cortical rather than poste-

Table 2. Post-stroke depression by side of lesion

	Left	Right	Odds ratio	95% CI
Major depression	8	12	0.6	0–1.6
Minor depression	7	6	1.1	0–2.3
All depressive disorders	15	18	0.7	0.1–1.5
Total patients	60	57		

Table 3. Classification of lesion location by associated post-stroke depression (major and minor depression combined)

	Left		Right	
	all patients	depression	all patients	depression
Cortical/subcortical				
Fronto-temporal	20	7	20	8
Parieto-occipital	8	2	8	3
Deep white matter	23	3	20	4
Deep nuclei	6	3	5	2
Posterior fossa	6	3	8	2
Total	63	18	61	19

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rior cortical lesions in left hemisphere strokes; (ii) left anterior lesions rather than right anterior lesions, and (iii) left anterior lesions rather than in any other lesion location in the brain, were tested. In doing so two different models of what constitued 'anterior' and 'posterior' lesions were tested, firstly defining anterior as the fronto-temporal areas listed in table 3, and secondly, a more restricted definition confirming the term 'anterior' to the frontal lobe only.

Fronto-Temporal. There was a greater proportion of depressed patients with left anterior (7/20, 35%) than left posterior (parieto-occipital) (2/8, 25%) lesions but these differences were not statistically significant. There was very little difference between the proportion of depressed patients between left (35%) and right (40%) anterior lesions. There was no support for the third of these hypotheses as (a) right anterior lesions were associated with a slightly higher proportion of depressed patients than were left anterior lesions, and (b) there were just as high, or higher, proportions of depression associated with other lesions, e.g. right parieto-occipital (37%), left deep nuclei (50%) and left posterior fossa (50%). None of these differences was statistically significant.

Frontal Lobes Only. There were very few lesions involving only the frontal lobes, namely 4 in the left side and 5 in the right. No cases of major depression were associated with frontal lobe lesions on either side, but there were 4 patients (2 each side) with minor depression. These small numbers do not allow the hypothesis to be meaningfully tested.

Overall, no matter which of the two definitions of 'anterior' lesion is adopted, it is clear that anterior lesions were associated with only a maximum of 40% of all post-stroke depressions and that there was no dominance of left anterior over right anterior lesions. When the analysis was confined to major depression only, there were no cases associated with left frontal lobe, insular/opercula, or right frontal lobe lesions. All 4 cases of major depression associated with left and 3 of the 4 associated with right 'fronto-temporal' lesions (table 3) were confined to lesions in the temporal lobe only.

A high proportion of lesions in the caudate/putamen/globus pallidus nuclei were associated with depression for both the left (3/5, 60%) and right (2/3, 67%) sides, but no patient with a lesion in the thalamus on either side (1L, 2R) was depressed. However, the numbers involved were very small.

It is concluded that the two null hypotheses postulated in the Introduction were sustained. No significant differences were found in the prevalence of post-stroke depression between patients with left and right hemisphere lesions, or between patients with lesions in any particular neuro-anatomically defined area of the brain.

Discussion

The results of this investigation have shown no significant difference in prevalence of depressive illness 4 months post-stroke associated with left and right cerebral hemisphere lesions. Using the method adapted for determining anterior and posterior locations of lesions, there was no difference between the prevalence of depression associated with anterior and posterior lesions in either hemisphere, or between left and right anterior lesions, or any dominance such as association of left anterior lesions over lesions in any other area of the brain. The prevalence of depression was similar for lesions in both left and right basal ganglia, namely the caudate, putamen and globus pallidus, but zero for the thalamus on both the left and right side. The latter was identical to the findings of Starkstein et al. [3].

As House et al. [18] have pointed out, there are a number of limitations of CT scanning as the means of locating lesions in studies of the outcome from stroke. Many patients with undoubted clinical evidence of a stroke have no corresponding lesion on CT scan [33], as shown by the large proportion (47%) of patient with first strokes in this study who did not have a lesion detected on CT. Furthermore, those patients with lesions on CT may also have vascular damage to other parts of the brain which does not show on the scan. Finally, although CT scans can accurately localise stroke lesions, dynamic studies show altered function in areas of the brain extending well beyond the visible lesion [34].

Why are the results of this study so different from those of Robinson's and some other investigators? It must be emphasised that this was not a replication of any of the previous studies. In adopting DSM-III criteria for major and minor depression we have used criteria for what constitutes a depressive illness that are essentially the same as those used by almost all investigators with the exception of the OCSP. However, the method employed to localise lesions on CT scans is basically different from most other studies, which have followed the topographical method devised by Robinson and his co-workers. An exception was the study by Dam et al. [35], but they only used the apportion of lesions to the left and right hemispheres in their analysis of association of lesion with depression. The considerable limitations of the method of localisation

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used by Robinson have been documented elsewhere [17, 21]. Particular concerns include the arbitrary nature of the method, its lack of definite relationship to neuroanatomical areas of the brain, and the fact that a designated anterior lesion may have the great bulk of its volume behind the posterior border of the anterior zone.

A central theme of most of the claims for a relationship between depression and lesion localisation has been the postulated great importance of lesions in the left anterior region of the brain. Hence we explored this hypothesis in this study as well as testing the other hypotheses of Robinson and co-workers. However, the definition used here of what constitutes an anterior lesion inevitably differs from the method of the localisation employed by the latter group. Particular difficulties were encountered in matching neuroanatomical areas to the somewhat arbitrary topographical method of localisation of the latter group, especially in establishing what they meant by 'cortical' vs. 'subcortical', and by 'anterior' vs. 'posterior' areas of the brain. Strictly speaking, the cortex is a relatively thin layer of grey matter on the outer surface of the brain and the white matter lying directly beneath could be termed subcortical. It would be only a very small and unusually placed lesion which involved the outer grey matter alone. Hence, in this sense, almost all cortical lesions involve some subcortical tissue. In the paper by Starkstein et al. [2] the term subcortical appears to refer to the deep nuclei (thalamus, caudate, putamen and globus pallidus). It is not clear which other neuroanatomical areas, other than the frontal lobe, and especially what part of the temporal lobe, are included in 'anterior'. One study [2] placed great importance on 'cortical or subcortical lesions involving at least part of the left dorsolateral frontal cortex', again creating some uncertainty.

The only two community-based studies which have attempted to study the postulated association of post-stroke depression and location of the cerebral lesion, namely the OCSP [8] and the PCSS, both found no evidence to support such an association. The other studies have been conducted on samples of hospital inpatients, or rehabilitation units. As House et al. [8] pointed out, this could create a bias, sometimes called Berkon's bias, where the location of the lesion might itself be associated with an increased risk of hospitalisation, or admission to a rehabilitation unit, because of the greater handicap associated with dysphasia or dominant limb weakness. Morris et al. [7], in acknowledging a possible methodological weakness of their study as all of their subjects came from a rehabilitation unit, stated that with a wider distribution of lesions, the relationship between anterior location and depression might be different. Another possible explanation raised by House et al. [8] is that there is a difference in the emotional behaviour of patients with left and right brain lesions, and other studies may not have sufficiently distinguished emotionalism associated with left stroke lesions from depressive illness. They found that emotionalism overlapped with, but was not synonymous with, psychiatrically diagnosable depression and was associated with anterior lesions. A careful distinction has been made between emotionalism and depression in both the Oxford and the Perth studies.

In this study there was a greater proportion of major than of minor depression in lesions in each hemisphere, especially on the right side. All hypotheses tested combined major and minor depression, thereby making no distinction between the two. This was done partly to increase numbers of depressed patients for analysis. Using two measures of depression, the PSE-ID-CATEGO and the Beck Depression Inventory, House et al. [8] showed that the scores were continuously rather than bimodally distributed, suggesting that the differences in depressive disorders in this population were a matter of degree rather than type. Similarly, separating the categories of major and minor depression according to the method of Starkstein and Robinson [9] has the same effect, namely seeing the differences as ones of degree or severity of depression rather than type of depression. Other investigators [7, 35, 36] have combined the major and minor depression in investigating location of lesion. Robinson's group have variously made a clear distinction between the two [3, 6] and combined the two in formulating their hypotheses and/or analysing the data, as did Eastwood et al. [36].

All of the previous studies have been characterised by small numbers of patients ranging from 35 [7, 37] to 92 [35]. Most of the investigations of Robinson and co-workers have ranged from 36 [1] to 45 [2], and therefore the major hypotheses linking PSD to site of lesion are built upon statistically unstable foundations. There were 117 patients in the PCSS, these being the only patients fulfilling the criteria from the 221 patients with first-ever stroke seen by the two psychiatrists. However, the modest numbers of patients could not be a tenable explanation for the failure to find any significant associations between location of lesion and depression in this study, as none of the differences were of a numerical order, or direction, to sustain the hypothesised associations. For example, there was a greater, but statistically insignificant, number of right than left hemisphere lesions associated with depression, a difference lying opposite in direction to that postulated by Robinson's group.

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In the PCSS 20 (32%) patients had left anterior lesions as defined by our neuroanatomical method, of whom 4 had major depression and 3 minor depression. Thus, only 19% of all depressed patients (19% major, 21% minor depression) had left frontal lesions. In these patients only 4 (3.5%) lesions (0 major and 4 minor depression) lay entirely in the frontal lobe. Thus, these figures represent only a minority of lesions and of depressed patients in the total cohort of patients studied.

Lesions in basal ganglia were associated with a high prevalence of depression in both hemispheres, whereas Starkstein et al. [3] reported greater prevalence in left ganglia lesions. The numbers involved in both studies were very small. The absence of any depression associated with thalamic lesions of either side was the only finding similar to that of Robinson's group, although again the number of thalamic lesions in each study was very small.

None of the methodological reservations discussed above can adequately negate the confirmation of the two general null hypotheses postulated at the beginning of this study, namely that there is no difference in the prevalence of PSD between patients with lesions in the left and right cerebral hemispheres, or in any particular neuroanatomically defined area of the brain within each hemisphere. In particular, there was no evidence to support the assertion that there is a significantly increased frequency of major depression associated with lesions in the left anterior brain rather than in any other part of the brain. On the other hand, on both sides of the brain, the prevalence of depression was very low with lesions involving the deep white matter and absent altogether in thalamic lesions.

There are a number of reasons other than site of lesion which may contribute to PSD and which should be considered in a study of the type reported in this paper. As far as we were able to assess at the 4-month post-stroke psychiatric examination, and at the initial post-stroke neurological examination by CSA, none of the 124 patients in this study had Alzheimer's disease or other forms of dementia prior to the stroke. Such conditions are known to be associated with high levels of depression. Patients depressed at the time of the stroke were excluded. Unfortunately, a detailed history of medication which might be associated with high depression levels was not obtained. At the 4-month examination only a small proportion of these patients were in residential care, a factor known to be associated with a high prevalence of depression. From our assessment it was clear that the reasons for residential care were not associated with their affective state but with their post-stroke disability and/or lack of adequate family support. Henderson et al. [38], in a study of the elderly in residential care in Canberra, found that the high level of depressive symptoms could not be attributed to exposure to these environments themselves, once account was taken of the higher level of physical morbidity compared to those in the community. We are currently preparing a paper on the 221 first-ever strokes [24] in the full Perth Community Stroke Study, examining as possible risk factors for PSD a number of demographic, social and other factors apart from site of lesion, e.g. MMSE, Barthel's Index, residential care, and physical status at the time of the stroke.

Conclusion

We found no support for the case for location of the lesion being a prime risk factor of PSD and advocate that future investigations of the aetiology of this disorder should encompass a much broader range of variables than location of the lesion. It is possible that a much larger number of subjects may have shown a statistical difference between left anterior and left posterior lesions in the prevalence of combined major and minor depression. Furthermore, close attention should be given to the number of subjects investigated to provide sufficient statistical power to fully test the hypotheses proposed. Reference was made earlier to the increasing emphasis on non-biological risk factors [13]. Additional areas for exploration include physical diseases which are highly associated with the onset of stroke and which themselves are associated with a high prevalence of depression, especially cardiovascular disorders and diabetes mellitus. The aetiology of PSD is likely to be multi-factorial and certainly much more complex than reflecting the location of the lesion, as advocated by Robinson et al. [1], or largely social factors, as surmised by House [14].

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