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Poststroke depression in obstructive cerebrovascular diseases of internal carotid and vertebrobasilar circulation system

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SOUHRN

Cíl: Cílem této studie bylo zkoumat neuroanatomické charakteristiky cerebrovaskulárního tepenného systému a hodnocení deprese po cévní mozkové příhodě při obstrukčním cerebrovaskulárním onemocnění postihujícím přední (vnitřních karotid) a zadní tepenné povodí (vertebrobazilární).
Materiál a metody: Do studie uspořádané s cílem posoudit korelaci mezi možnými rizikovými faktory a incidencí deprese po cévní mozkové příhodě (poststroke depression, PSD) bylo zařazeno 105 pacientů s PSD. Jednalo se o 58 (55,2 %) žen a 47 (44,8 %) mužů průměrného věku 61,3 ± 10,2 roku. Zaznamenávaly se demografické údaje, komorbidity a neurologické symptomy. Zkoumala se korelace PSD s následujícími faktory: strana postižení a konkrétní oblast vzniku cévní mozkové příhody. Ke klasifikaci účinků poškození mozku se používala stupnice Disability Rating Scale. Kognitivní stav se hodnotil pomocí krátkého testu kognitivních funkcí (Mini Mental State Examination, MMSE). Diagnóza deprese se stanovovala s použitím kritérií DSM-III-R. Jako nástroje pro stanovení závažnosti deprese se používaly Hamiltonova posuzovací stupnice deprese (Hamilton Depression Scale) se 17 položkami a Beckova stupnice deprese (Beck Depression Scale) s 21 položkami během prvního měsíce po cévní mozkové příhodě.
Výsledky: Většina pacientů (81,9 %) měla klinické rizikové faktory jako hypertenzi, diabetes mellitus a ischemickou chorobu srdeční. Hypertenze jako hlavní rizikový faktor byla přítomna u 64,8 % pacientů. Kuřáctví v anamnéze uvedlo 60,9 % pacientů. Průměrná hodnota zdravotního postižení byla 2,9 ± 1,2 u 55 pacientů bez PSD a 3,7 ± 1,1 u 50 pacientů s PSD ($p < 0,05$). Průměrná hodnota na stupnici MMSE činila 27,4 ± 1,5 u 55 pacientů bez deprese po cévní mozkové příhodě a 24,7 ± 2,3 u 50 pacientů s depresí po cévní mozkové příhodě ($p < 0,05$). U 70 pacientů bylo dominantní postižení karotického tepenného systému (vnitřní karotidy) a u 35 dominantní postižení vertebrobazilárního tepenného systému. Při srovnání obou pohlaví podle převládající oblasti postižení (předního nebo zadního) byly okluzivní léze zjištěny na systému karotid u 40 žen (38,1 %) a 30 (28,6 %) mužů, zatímco okluzivní léze vertebrobazilárního systému byly nalezeny u 18 žen (17,1 %) a 17 mužů (16,2 %). Mezi podskupinami nebyly zjištěny žádné statisticky významné rozdíly.
Závěr: Naše studie nepotvrdila jakoukoli souvislost mezi depresí po cévní mozkové příhodě a oblastí léze na mozku. Další výzkum se musí zaměřit na klinické a neuroanatomické projevy umožňující popsat vztah mezi PSD a oblastí léze.

ABSTRACT

Objective: The aim of this study was to investigate the neuroanatomic feature of cerebrovascular circulation and the rating of poststroke depression in obstructive cerebrovascular disease involving anterior (internal carotid) and posterior (vertebrobasilar) systems.
Materials and methods: One hundred and five patients with poststroke depression (PSD), 58 (55.2%) women and 47 (44.8%) men, mean age 61.3±10.2 years were enrolled in the study for correlation between potential risk factors and the incidence of poststroke depression (PSD). Demographic data, comorbidities and neurological symptoms were recorded. The correlations of the PSD with the factors: the side and site of brain infarcts, and the origin of cerebral circulation site were investigated. Disability Rating Scale was used to rate the effects of cerebral injury. Mini Mental State Examinations were applied to evaluate the cognitive state. Depression was diagnosed using DSM-III-R criteria. To measure the severity of depression, 17-item Hamilton Depression Scale and 21-item Beck Depression Scale were used within the first month of stroke.
Results: Most of the patients (81.9%) had clinical risk factors as hypertension, diabetes mellitus, ischemic heart disease. Hypertension was identified in 64.8% of the patients as the major risk factor. Smoking history was reported by 60.9% of the patients. The mean disability rating scale was 2.9±1.2 in 55 patients without PSD and 3.7±1.1 in 50 patients with PSD ($p < 0.05$). The mean Mini Mental State Examination (MMSE) was

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found 27.4±1.5 in 55 patients without poststroke depression, and 24.7±2.3 in 50 patients with poststroke depression (p <0.05). Seventy patients had anterior (internal carotid) circulation system and 35 patients had posterior (vertebrobasilar) circulation system dominantly. Comparing with the patient's gender according to anterior or posterior system dominancy, 40 female (38.1%) and 30 (28.6%) male patients suffered from internal carotid system occlusive lesions and 18 female (17.1%) and 17 male (16.2%) patients suffered from vertebrobasilar system occlusive lesions. There was no statistically significant differences between the subgroups.

Conclusion: Our study did not confirm any association between depression after stroke and brain lesion location. Future efforts should aim to enhance clinical and neuroanatomical studies for investigating the relationship between PSD and lesion location.

Introduction

Stroke is defined as a sudden loss of blood supply to the brain leading to permanent tissue damage caused by thrombotic, embolic, or hemorrhagic events.[1] Almost 85% of strokes are ischemic, while 15% are hemorrhagic. Patients with brain injury could change, or even lose, some of their functions (e.g. language, cognition, emotion, awareness, social function). Stroke as the most common disabling disease and one of a leading cause of death has an enormous emotional impact on both patients and their family members. Patients after stroke have worse functional outcomes and quality of life. Depression is a common neuropsychiatric consequence of stroke.[2]

Poststroke depression (PSD) is among the most frequent emotional disorders afflicting stroke sufferers. Poststroke depression could be defined as a depression occurring in the context of a clinically apparent stroke. Approximately one third of stroke survivors experience an early or later onset of depression. Its prevalence has been estimated to be around 30–35%, ranging from 20 to 60%.[3]

The association of neuropsychiatric disorders with cerebrovascular disease includes depression, anxiety disorder, apathy, cognitive disorder, mania, psychosis, pathological affective display, catastrophic reactions, fatigue, and anosognosia. The stroke itself poses the risk of depression. Stroke survivors are more predisposed to PSD compared to physically ill patients with similar levels of disability, even quite a long time after the stroke, regardless of other risk factors. The interaction between depression and stroke is very complex. The pathophysiological mechanisms have not been fully elucidated yet, nevertheless an interaction between neuroanatomical and psychosocial factors may be important in PSD development.[4–8] The relationship between the neuroanatomic locations of brain damage depending on cerebrovascular circulation whether carotid or vertebrobasillary origin and the incidence of PSD has not been defined and elusidated completely. With the purpose of gaining a consistent, strong, and credible conclusion on the relationship between PSD, some studies have investigated this relationship but the evidence has been still conflicting.[9]

The aim of this study was to investigate clinical characteristics of patients after stroke with single stroke lesions, no prior history of psychiatric disorder and to determine the poststroke depression risk and to analyse relationship of location of the brain lesion and neuroanatomic feature of cerebrovascular systems from anterior (internal carotid) and posterior (vertebrobasilar) circulation.

Materials and methods

One hundred and five patients, 58 (55.2%) women and 47 (44.8%) men, mean age 61.3±10.2 years (22–80), were enrolled in the study for correlation between potential risk factors and the 1-year incidence of poststroke depression (PSD).

For the stroke location of the patients, whether it belongs to the anterior or posterior cerebrovascular system was determined using the computed tomography. The study population comprised of randomly selected 105 patients admitted for to treatment of occlusive cerebrovascular disease in one year. Patients with a consciousness level suitable for psychiatric and cognitive evaluation and diagnosed with obstructive cerebrovascular disease radiologically were included in the study. Specific exclusion criteria included unconsciousness, motor or sensorial aphasia, dysarthria preventing psychiatric interview, a history of previous stroke, a history of previous depressive or psychiatric episode in medical history. Also the patients with infact lesions in both hemispheres and both anterior (internal carotid) and posterior (vertebrobasilar) systems were excluded from the study.

Sociodemographic data on age, gender, marital status and education level were recorded. Patient-related factors and comorbidities (hypertension, diabetes mellitus, ischemic heart disease, smoking), neurological symptoms, functional disability and cognitive deficits were recorded. For neuroimaging and stroke location of the patients, whether it belongs to the anterior or posterior cerebrovascular system was determined using the computed tomography scans (CT). The correlations of the depression development after ischemic stroke were investigated systematically with the following factors: the side and site of brain infarcts, and identifying the origin of cerebral circulation site. Anterior circulation and posterior circulation blood supply areas were evaluated according to Hanna Damasio's brain blood supply mapping. Computed tomography studies of depressed patients have revealed structural abnormalities in cortical and subcortical areas related to limbic-cortical-striatal-pallidal-thalamic-cortical pathways, including the frontal lobes, caudate, and putamen. Localization of the infarcted area was enrolled based on the site of lesion as cortical, subcortical, cerebellum and brain stem.

A range of demographic, clinical, radiological and poststroke depressive characteristics was collected and analyzed as potential determinants of outcome. The important study characteristics were determined and recorded within the first month of stroke, and the effect sizes of the relationship between PSD and lesion location were statistically analysed.

The patients' disability was assessed, including the impairment and handicap of an individual. Disability Rating Scale (DRS) was used to rate the effects of cerebral injury (no significant disability, mild disability, moderate disability, moderate to severe disability, severe disability). The rating gave insight into the cognitive impairment of the individual. Mini Mental State Examination (MMSE) was applied to evaluate the cognitive function.

The association between the cerebrovascular changes and depression, also more specifically the location of brain lesion as a result of stroke and depression has been analyzed. Psychiatric evaluation was made within the first month after the emergence of stroke. The SCID-NP (Structured Clinical Interview Non-Patient) clinical interview form, which was structured based on DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, 1987 revision) diagnostic criteria published by the American Psychiatric Association[10] was administered to the patients in the study group. Depression was diagnosed using DSM-III-R criteria. To measure the severity of depression, 17-item Hamilton depression scale[11] and 21-item Beck Depression Scale were used.[12] Beck Depression Scale was read to all patients.

All those who participated in the study signed the informed consent. The study was performed according to the principles of the Declaration of Helsinki.

Diagnosis of poststroke depression

Estimation of depression in evaluating patients after stroke, depression rating scales are necessary for the quantification and monitoring of depressive symptoms. A patient with a diagnosis of depression due to stroke must have depressed mood or loss of interest or pleasure along with symptoms of depression lasting two or more weeks.

The Hamilton Depression Scale (HAM DS) originally developed and published by Max Hamilton in 1960, is a multiple item questionnaire used to provide an indication of depression and as a guide to evaluate recovery.[11] The original 1960 version questionnaire with 17 items is designed and revised for adults and is used to rate the severity of their depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss, and somatic symptoms. The application time of the test is approximately 20 minutes. The original 1960 version contained 17 items, but four other questions not added to the total score were used to provide additional clinical information. Each item on the questionnaire is scored on a 3- or 5-point scale, depending on the item and the total score is compared to the corresponding descriptor. A version translated into Turkish was used.

The Beck Depression Inventory (BDI), originally developed and published by Aaron T. Beck in 1961, is a 21--item self-assessment psychometric test that measures characteristic attitudes and symptoms of depression.[12] The Beck depression inventory takes approximately 10 minutes to complete, although clients require a fifth–sixth grade reading level to adequately understand the questions. When the test is scored, a value of 0 to 3 is assigned for each answer and then the total score is compared to a key to determine the depression's severity. Higher total scores indicate more severe depressive symptoms. The standard cut-offs are as from 0–9 points and indicate minimal depression to 30–63 indicates severe depression. A version translated into Turkish was used.

Statistical analysis

Descriptive statistics were used to summarize the demographic, clinical, and radiological variables. Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between groups. Patient population was categorically divided into diagnostic groups of those with or without depression. Data are expressed as mean values ± standard deviation for continuous variables and as numbers with percentage for categorical variables. The discrete variables were compared using the χ^2 test and continuous variables were compared using a two-tailed *t* test. Differences obtained from the without PSD and with PSD assessments were compared by Wilcoxon matched-pairs rank-sum test. Nearly, 95% confidence interval has been computed to find the significant features. *P* value was set at ≤ 0.05.

Statistical analysis was performed using the Statistical Package for the Social Sciences SPSS 15.0 for Windows (SPSS Inc., Chicago, IL).

Results

The study group consisted of one hundred and five patients, 58 women (55.2%) and 47 men (44.8%) with a mean age 61.3±10.2 years (ranged 22–80). 78 of the 105 patients were married (74.3%) with the average number of children 3.3±1.6.[1–8] The mean education year was 6.8±4.6 (ranged 0–19). Sociodemographic data on age, gender, marital status, education level and patients' dominant hand were recorded (Table 1).

Comorbidities were assessed as the risk factors of cerebrovascular disease. Most of the patients (81.9%) had clinical risk factors as hypertension, diabetes mellitus, ischemic heart disease. Hypertension was found in 64.8% of the patients as the major risk factor. Reported smoking history was 60.9% of the patients. Clinical risk factors, neurological symptoms, functional disability, cognitive deficits and localization of occlusive lesions were evaluated and summarized in Table 2.

Poststroke depression was assessed within first month after stroke. For the diagnosis of depression, enrolled 17-item Hamilton Depression Scale and 21-item Beck Depression Scale indicated that 55 patients were diagnosed

Table 1 – The patients characteristics

	n	%
Age		
Mean (years)	61.3±10.2 (22–80)	
21–30	1	1.0
31–40	2	1.9
41–50	12	11.4
51–60	31	29.5
61–70	44	41.9
71–80	15	14.3
81 and older	–	
Gender		
Female	58	55.2
Male	47	44.8
Marital status		
Mean (number of children)	3.3±1.6 (1–8)	
Married	78	74.3
Single	2	1.9
Widow/widower	25	23.8
Education level		
Primary school and lower	43	40.9
Secondary school	48	45.7
High school	11	10.5
University and higher	3	2.9
Dominant hand		
Left	89	84.8
Rigth	11	10.5
Both	5	4.8

Table 2 – Clinical characteristics

	n	%
Comorbidities		
Hypertension	68	64.8
Diabetes mellitus	27	25.7
Ischemic heart disease	32	30.5
Without comorbidities	19	18.1
Smoking history	62	59.0
Alcohol	24	22.9
Alcohol + smoking history	2	1.9
Other	14	13.3
Non	3	2.9
Neurological symptoms		
Facial impairment	81	77.1
Upper extremity impairment	90	85.7
Lower extremity impairment	89	84.8
Visual defect	36	34.3
Brainstem-cerebellar signs	25	23.8

Table 2 – Clinical characteristics

Degree of functional disability		
No significant disability	8	7.6
Mild disability	26	24.8
Moderate disability	18	17.1
Moderate to severe disability	38	36.2
Severe disability	15	14.3
Localization of occlusive lesion		
Left hemisphere	48	45.7
Anterior system	40	38.1
Posterior system	8	7.6
Right hemisphere	37	35.2
Anterior system	30	28.6
Posterior system	7	6.7
Cerebellum and brain stem	20	19.0

without PDS, and 50 patients with PDS. Predictors of poststroke depression, age, gender, level of education, prestroke life conditions and events, comorbidity and risk factors, stroke location, severity of disability, impairment of cognitive capability were compared between the groups without and with PDS in Table 3. The mean disability rating scale was 2.9±1.2 in 55 patients without PSD and 3.7±1.1 in 50 patients with PSD (p <0.05). The mean Mini Mental State Examination (MMSE) was found 27.4±1.5 in 55 patients without poststroke depression, and 24.7±2.3 in 50 patients with poststroke depression (p <0.05).

In the study, the prevalence of major depression was found to be 47.6%. The localization of infarcted lesions and the stroke characteristics were listed in left hemisphere of brain in 48 patients, in right hemisphere of brain in 37 patients, cerebellum and brain stem in 20 patients. was not associated with PSD. Lesion location implied that PSD was associated with left-side lesions, but the association was not statistically significant (Table 4).

The poststroke depression characteristics and the mean depression rating scales correlation with cerebrovascular circulatory characteristics were compared between the subgroups in Table 5. There was not found any statistically significant difference between female and male patients, also between left and right hemispheres.

In the group, 70 patients had anterior (internal carotid) circulation system and 35 patients had posterior (vertebrobasilar) circulation system dominantly. Comparing with the patient's gender according to anterior or posterior system dominancy, 40 female (38.1%) and 30 (28.6%) male patients suffered from internal carotid system occlusive lesions and 18 female (17.1%) and 17 male (16.2%) patients suffered from vertebrobasilar system occlusive lesions. There was no statistically significant differences between the subgroups (Table 7). Our study did not confirm any association between depression after stroke and brain lesion location.

Table 3 – The distribution of risk factors of groups					
	Without PSD		With PSD		
	55 patients	(52.4%)	50 patients	(47.6%)	*p*
	n	%	n	%	
Age					
Mean	66.7±8.4		58.8±7.8		ns
Gender					
Female	27	46.6	31	53.4	ns
Male	28	59.6	19	40.4	ns
Education level					
Primary school and lower	20	36.5	23	46	ns
Secondary school	26	47.6	22	44	ns
High school	6	10.5	5	10	ns
University and higher	3	5.4	0	0.0	ns
Comorbidities					
Hypertension	29	27.6	39	37.1	ns
Diabetes mellitus	11	10.5	16	15.2	ns
Ischemic heart disease	18	17.1	14	13.3	ns
Without comorbidities	13	12.4	6	5.7	ns
Smoking history	34	61.8	28	56.0	ns
Alcohol	14	25.6	10	20	ns
Alcohol + smoking history	1	1.8	1	2	ns
Other	5	9.1	9	18	ns
Non	1	4.8	2	4	ns
Functional disability (DRS)					
Mean	2.9±1.2		3.7±1.1		$p < 0.05$
Cognitive deficits (MMSE)					
Mean	27.4±1.5		24.7±2.3		$p < 0.05$

DRS – Disability Rating Scale; MMSE – Mini Mental State Examination.

Table 4 – The distribution of the infarcted area in brain tissue				
	Without PSD		With PSD	
	55 patients		50 patients	
	n	%	n	%
Left hemisphere (anterior system)	18	32.7	22	44.0
Cortical	11	20.0	7	14.0
Subcortical	4	7.3	11	22.0
Cortical + subcortical	3	5.4	4	8.0
Right hemisphere (anterior system)	16	29.1	14	28.0
Cortical	5	9.1	9	18.0
Subcortical	6	10.9	4	8.0
Cortical + subcortical	5	9.1	1	2.0
Left hemisphere (posterior system)	4	7.3	4	8.0
Cortical	3	5.5	4	8.0
Cortical + subcortical	1	1.8	-	0.0
Right hemisphere (posterior system)	7	28.6	-	0.0
Cortical	4	7.3	-	0.0
Cortical + subcortical	3	5.5	-	0.0
Left cerebellum	3	5.5	2	4.0
Right cerebellum	2	3.6	2	4.0
Left brain stem	3	5.5	4	8.0
Right brain stem	2	3.6	2	4.0

PDS – poststroke depression.

Limitations

The limitation of this study is that demographic and clinical variables are not included in the regression analysis due to the limited number of cases. Future multi-case studies should examine demographic, clinical and anatomical variables and psychiatric health status as predictors of benefits recovery from stroke. Metaanalysis might lead the overall effect size obtained to reach statistical significance.

Table 5 – Poststroke depression characteristics

	Female	Male	*p*
Depression diagnosis			
Without PSD	n = 28 (%)	n = 19 (%)	ns
With PSD	n = 27 (%)	n = 31 (%)	ns
Hamilton Depression Scale			
No. of patients	58 (55.2%)	47 (44.8%)	ns
Mean	19±12.2	17±12.3	ns
Beck Depression Scale			
No. of patients	58 (55.2%)	47 (44.8%)	ns
Mean	21.6±13.6	18.3±12.7	ns
	Left hemisphere	**Right hemisphere**	*p*
Hamilton Depression Scale			
No. of patients	43 (58.1%)	31 (41.9%)	ns
Mean	18.8±12.7	17.8±11.5	ns
Beck Depression Inventory			
No. of patients	43 (58.1%)	31 (41.9%)	ns
Mean	21.9±13.7	19.3±12.8	ns

Table 6 – The cerebrovascular systems characteristics of patients with poststroke depression

	Anterior S		Posterior S		*p*
	70 patients		35 patients		
	n	%	n	%	
Age					
Mean	62.3±8.4		57.8±10.1		ns
Gender					
Female	40	57.1	18	51.4	ns
Male	30	42.9	17	48.6	ns
Disability (DRS)					
Mean	3.3±1.2		3.2±1.2		ns
Cognitive state (MMSE)					
Mean	25.9±2.5		326.7±1.8		ns
Depression (PSD)					
Without PSD	34	48.6	21	60	ns
With PSD	36	51.1	14	40%	ns
HAM DS					
Mean	19.0±12.6		16.2±11.3		ns
BDI					
Mean	21.5±13.6		17.2±12.4		ns

BDI – Beck Depression Inventory; DRS – Disability Rating Scale; HAM DS – Hamilton Depression Scale; MMSE – Mini Mental State Examination; PDS – poststroke depression.

Discussion

Poststroke depression (PSD) is of high clinical importance. Poststroke depression interferes with rehabilitation from stroke, negatively affects quality of life and may be responsible for poor outcome of stroke with increased morbidity and mortality. Gold standard for the diagnosis of depression represents the DSM-IV and DSM-V criteria.[13,14]

Our understanding of the relationship between the brain damage and the incidence of PSD is not complete. PSD represents a multi-factorial pathological condition, and both psychological and biological factors may influence its development.[9] Predictors related to PSD are constitutional (age, female gender), clinical (previous stroke, previous depressive or psychiatric episode, cognitive impairment or aphasia), functional (severity of disability); environmental (premorbid neurotic personality and social isolation), biological (family history of depression, both genetic and environmental – double biological hit).[3,15,16] Other risk factors such as education level, previous stroke, stroke severity, apathy, denial reaction at the acute stage, cerebral atrophy have been alternatively found to be associated with PSD.[16] Early effective treatment of depression may have a positive effect not only on depressive symptoms but also on the rehabilitation outcome of stroke patients. On the other hand, there is no definitive evidence that antidepressants or psychotherapy are useful to prevent depression. Implementing preventive and therapeutic strategies to reduce the risk of mood alteration and thus improve rehabilitation outcomes would appear important in the organization of stroke services.

During the past several years we have been studying mood changes in stroke patients. The clinical parameters were reported to be associated with PSD, higher age[17] but also younger age,[18] stroke severity, and physical disability resulting from stroke. A systematic review of studies of stroke patients reported that gender was not found a significant risk factor for PSD.[19,20] Further predictors of PSD comprise a history of psychiatric disease, especially previous depression,[17,21] but also social isolation,[19,22] level of education,[16,21] institutionalization after stroke,[23] or stressful life events before stroke.[17,24] Multiple factors including severity of impairment and quality of social supports contribute to the development of poststroke depression. The available evidence concerning PSD and social support is conflicting, probably because of significant heterogeneity in the definition and evaluation of social support.[2] The frequency of PSD has been published in many countries of the studies. The most quoted studies of prevalence and incidence of PSD have utilized meta-analysis to create large databases.[21]

Recently, modern approaches of localizing stroke lesions with reference to standard brain atlases and of voxel-based analysis have been applied in studies of PSD. Voxel-based symptom lesion mapping in PSD research involves lesion segmentation on high-resolution brain imaging.[25]

In recent years, there has been an interest in modeling of neuropsychiatric consequences of stroke for early identification of patients at the highest risk poststroke depression and those most likely to benefit from prophylactic and treatment interventions.[26] Neurochemical changes and clinical findings are similar to endogenous

depression. Although PSD is potentially treatable, the efficacy of preventive strategies in PSD remains essentially undetermined.[27]

One etiological theory for depression after stroke is that it is a psychological reaction to the clinical consequences of stroke. The hypothesis of vascular depression refers to the concept of vulnerability to depressive symptoms resulting from structural brain damage caused by cerebrovascular disease mainly in elderly people.[28] Some researchers even argue that PSD is a kind of vascular depression because both diseases involve depressive symptoms that are both symptoms and a cause of cerebrovascular disease. The hypothesis of an association of stroke lesions to PSD was observed in the relation of focal damage to the brain leading to psychiatric symptoms.[29] On the other hand, vascular depression rather affects small vessels and silent brain infarctions can be seen; whereas in PSD, the patient, by definition of stroke, is symptomatic and often larger brain vessels are affected.

Another theory was the depletion of monoaminergic amines occurring after stroke plays a role in PSD.[30] Norepinephrinergic and serotoninergic pathways are disrupted in the basal ganglia and frontal lobe lesions – sites that are shown to be associated with PSD.[31] When looking at the type of depressive disorder, PSD appears more to act like an endogenous depression than vascular depression. Serotonine and its metabolites showed a more or less opposite pattern, so the authors suggest that these data reflect the anatomical and functional subdivision of the monoamine network into two specific components, i.e., catecholamine (noradrenaline and dopamine) and serotonine.[32] Lesions involving the basal ganglia are more prone to lead to PSD.[31,33]

The potential effect of using different assessment tools and different assessors in the evaluation of PSD were investigated.[34] No evidence supported the hypothesis that the time between stroke and diagnosis of depression was an important confounder. Lesion location was not associated with depression no matter when the depressive symptoms after stroke were assessed. Brain damage secondary to stroke may play a less dominant role in the development of changes in mood and emotion.

To the effect of the interaction between lesion location and lesion volume on PSD, contradictory findings were reported.[35,36] Although the studies claimed that investigation of the relationship between depression after stroke and brain lesion location were similar; definitions of disease, diagnostic criteria, types of depression rating scales and assessment time were different due to methodological problems. Many studies have investigated this relationship and the evidence is conflicting. Severity of PSD was reported to be associated with lesion location[37] but not with lesion size.[22]

Laterality was one of the first characteristics of stroke lesions reported to be linked to symptoms of PSD with symptoms of depression observed more frequently in right hemispheric.[38] There are, however, studies with contradictory finding, an association of left hemispheric lesions with higher prevalence and severity of PSD.[4,17]

Many of the studies conducted by Robinson, scholastic viewpoints, and textbooks support the association between depression and left-hemisphere lesions.[2,4–8] In contrast, some studies suggest the opposite result, that depression is associated with right-hemisphere lesions.[34] Other studies do not confirm any association between depression after stroke and brain lesion location.[39,40] The association between the vascular changes and depression and more specifically the location of brain lesion as a result of stroke and depression has been identified as specific relationships between the locations of brain ischemic injury.[41]

The systematic reviews of this topic did not substantiate any definitive statement about the relationship between location of stroke lesion and risk of depression.[42] In most of the studies, patients with left hemisphere damage had been excluded from samples because of the language comprehension or expression difficulties caused by stroke. The existence and severity of depression in patients with left hemisphere damage may be underestimated, which in turn yielded the result that depression was associated with right hemisphere lesions. The studies have shown that patients with left hemisphere lesions have higher depression scores than those with right hemisphere lesions. However, intrahemispheric lesion location seems to have as great impact as interhemisphere lesion location. Patients with left anterior lesions were significantly more depressed than patients with left posterior lesions even if the patient had bilateral lesions.[43]

Previous studies suggested that causal relationship may exist for lesions at certain locations, including the left frontal lobe, the left basal ganglia, lateral frontal cortex, right hemisphere and occipital lobe.[2,4–8] The cortical–subcortical area in the frontal lobe, anterior limb and genu of internal capsule are included in the prefrontal-subcortical circuit, while the cortical–subcortical area in the temporal lobe and the posterior limb of internal capsule are included in the fronto-limbic-striatal circuit. These two circuits, which play important roles in the formation of emotion, cognition and behavior control,[44] have also been investigated in many studies about their roles in primary depression and post-stroke depression. Yu published that PSD was slightly associated with right-side lesions,[45] while Carson showed no association.[34] Instruments were originally developed for use in non-brain-damaged patients and have not been adapted to take into account the ways in which the symptoms of brain damage may affect and alter the clinical presentation of depression.[45] These methods should be specifically validated for neurologically impaired populations.

Due to the possible changes in self-awareness, language expression, interpersonal interaction, emotion, personality, or physical functioning, assessment results become biased or cannot be applied.[46,47] Patients with brain injury could change, or even lose, some of their functions (e.g. language, cognition, emotion, awareness, social function). These traditional diagnostic criteria or brain lesion location and stroke severity can be diagnosed by instruments, depression assessment cannot be complete without the use of language. While reviewing the literature, brain lesion location and stroke severity can be diagnosed by instruments, depression assessment cannot be complete without the use of language.[46,47] Taking into consideration that different stroke damage features directly or indirectly influence the accuracy of depression diagnosis, in our study, stroke patients who suffered from aphasia were excluded.

This lack of association is hardly surprising given the heterogeneity in the way in which depression was assessed in these studies, the diverse timing of the assessments, the different definitions of lesion location. All available studies on the association of stroke lesions and PSD are restricted from a number of methodological limitations.[48] If successful treatment can be instituted, rehabilitation may be shortened, costs reduced, quality of life improved, and unnecessary premature deaths prevented.

Conclusion

In conclusion, understanding of the relationship between neurological damage and depression after stroke would provide insight into the neurobiology of depression. The diagnosis of PSD is challenging and also because of their impact on quality of life, PSD should be promptly recognized and treated. The clinical studies on ischemic stroke patients have suggested that certain neuroanatomical factors may correlate with the PSD development. On the basis of our study results, we suggest that multiple information sources, multidimensional neuropsychologic assessment and neuroimaging techniques to reduce to morbidity and mortality. Future efforts should aim to enhance clinical and neurophysiological studies for investigating the relationship between PSD and lesion location underlying mechanisms interacting between lesion location and PSD and how to effectively help patients to become healthy.

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