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Stroke Lesions and post-stroke depression among survivors in Ibadan, Nigeria

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Abstract

Background: We aimed to determine the association between the neuro-radiological characteristics of stroke lesions and post-stroke major depression among survivors in Ibadan, Nigeria. This is in the background of a paucity of information on the clinico-pathological correlation of post-stroke emotional responses among African Survivors.

Method: We studied 30 stroke survivors receiving physiotherapy. The radiological characteristics of the stroke lesions were documented using computerized tomography or magnetic resonance imaging scans in the acute phase of the stroke. While the presence of major depressive disorder meeting criteria in the fourth edition of the Diagnostic and Statistical Manual was assessed using the Schedule for Clinical Assessment in Neuropsychiatry (SCAN), between 3 months and 2 years after. The association between lesion characteristics and depression was explored using logistic regression analysis.

Result: Nine (30.0%) stroke survivors met criteria for major depressive disorder. There were significant differences in their gender. The differences in the lesion types approached the set level of significance in survivors with or without major depressive disorder. There were however no differences when considering hemispheric lateralization or intra-hemispheric lesion location. Being female, but not the lesion characteristics was strongly associated with post-stroke major depressive disorder

Conclusion: Lesion characteristics documented in the acute phase of stroke could not predict the occurrence of major depressive disorder during rehabilitation in this sample. The occurrence of depression among stroke survivors may ultimately be determined by a combination of factors.

Keywords: *Stroke lesions, post-stroke, survivors, depression*

Résumé

Contexte : Nous visant à déterminer l'association entre la neuro-radiologiques caractéristiques de course et les lésions post-course dépression majeure parmi les rescapés à Ibadan, Nigéria. C'est dans le contexte de la pénurie d'informations sur la clinique-pathologiques de corrélation post-course réponses émotionnelles africains parmi les survivants.

Méthode : Nous avons étudié 30 course survivants reçoivent la physiothérapie. Les caractéristiques radiologiques de l'accident vasculaire cérébral lésions ont été documentées par tomodensitométrie ou l'imagerie par résonance magnétique numérise dans la phase aiguë de l'accident vasculaire cérébral. Tandis que la présence de troubles dépressifs majeurs répondant aux critères de la quatrième édition du Manuel diagnostique et statistique a été évaluée à l'aide du calendrier d'évaluation clinique de neuropsychiatrie, entre 3 mois et 2 ans après. L'association entre lésion caractéristiques et la dépression a été exploré moyen d'analyses de régression logistique.

Résultat: Neuf (30,0 %) course survivants répondait aux critères de trouble dépressif majeur. Lere eu des différences importantes dans leur sexe. Les différences dans la lésion types approchés du jeu au niveau de signification de survivants avec ou sans troubles dépressifs majeurs. Il n'y avait cependant pas de différences lorsque l'on examine l'hémisphère lateralization ou intra-hémisphérique emplacement de la lésion. Étant des filles, mais pas les caractéristiques de la lésion a été fortement associé avec post-course trouble dépressif majeur

Conclusion : lésion caractéristiques documentées dans la phase aiguë de la course ne pouvait prédire l'apparition de troubles dépressifs majeurs au cours de la période de réadaptation dans cet échantillon. L'apparition de la dépression chez course survivants peuvent, en fin de compte, déterminé par une combinaison de facteurs

Introduction

Stroke is widely regarded as the leading cause of long-term adult disability world-wide [1-3]. Apart from the more dramatic motor disabilities, impairments in social and mental dimensions of functioning are also often present [4]. Post-stroke

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depression is particularly common [5-6], and contributes much to the general morbidity burden of stroke [7-8]. It has long been viewed as a psychological reaction to physical disability and the psycho-social stress surrounding the stroke event [9-10]. But psychological disturbances are not specific to stroke, as such events have been shown to precede the onset of idiopathic depression as well as many other physical and mental disturbances [10-11].

Several lines of research have also suggested links between biological risk factors for sub-clinical brain injuries predating a stroke and depression [12-14]. In line with such biological hypotheses are findings from some clinico-pathological correlation studies that the location of the stroke lesion is an important factor in post-stroke depression [15-16]. The findings of these studies have not been replicated consistently in systematic reviews and meta-analyses of the literature on post-stroke depression and lesion location [6, 16-17]. Nevertheless, the notion that emotional response to a stroke event is lateralized remains popular.

In the midst of the inconsistent findings in the several attempts at investigating this hypothesis is the possibility that significant methodological differences exist in the studies analyzed. It has also been argued that the anatomical correlates of post-stroke depression may change over time, probably because of the healing process or the psycho-social adjustment of the stroke survivors to their difficulties [18]. Such changes may ultimately influence the presence or absence of lateralization in the emotional response to stroke in a sub-set of survivors [19-20].

Despite the enormous volume of research papers on clinico-pathological correlation of post-stroke depression and lesion location worldwide, there are no data from the African population. Yet studies of this kind are long overdue. This is particularly so in Nigeria, a country that is potentially home to the largest population of indigenous African stroke survivors. Clinico-pathological correlation studies of post-stroke depression and lesion location may be especially important as they have the potentials to provide a basis for the explanation of more subtle neuro-pathology in patients with primary mood disorders, as well as in geriatric depression. The present study was designed to bridge the existing knowledge gap in this area among African stroke survivors. We aimed to explore the association between neuro-radiological characteristics of stroke lesions and major depression diagnosed according to the criteria of the fourth edition of the Diagnostic and Statistical Manual (DSM IV) [21] among stroke survivors in Ibadan, Nigeria.

Method

Subjects

The study population comprised of a sample 30 adult stroke survivors with neuro-imaging done during the acute phase of the stroke. They were consecutively recruited from the physiotherapy clinic of the University College Hospital, Ibadan, between May and October 2010. The diagnosis of stroke was made according to the World Health Organisation (WHO) criteria, in which stroke is defined as "a sudden onset of focal or global neurological dysfunction that is of no other cause than vascular and which results in death or lasts more than 24 hours" [22-23]. We included only survivors with first stroke occurring between 3 months and 2 years before assessment for depression. This is because post-stroke depression has been reported to be commoner between 3 and 24 months post-stroke [24]. Participants were those who had brain Computerized Tomography (CT) or Magnetic Resonance Imaging (MRI) scan within the first week after the stroke. Patients with a history of recurrent stroke or diagnosis of dementia were excluded. Also excluded were patients with surgically treatable lesions on CT or MRI scan (e.g subdural haematoma, hydrocephalus and brain tumours). Those with other Central Nervous System (CNS) conditions that can cause depression (e.g Parkinson's disease), comorbid illnesses (e.g, chronic kidney disease, metastatic cancer, open tuberculosis, AIDS complex), as well as a previous history of psychiatric disturbances or treatment were additionally excluded. A further exclusion criterion was the inability of a survivor to communicate reliably because of aphasia.

Informed consent was obtained from all subjects. Ethical approval to undertake the study was obtained from the Joint Ethical Committees of the University of Ibadan and the University College Hospital Ibadan.

Study instruments

The schedules for clinical assessment in Neuropsychiatry (SCAN).

Diagnosis of major depression was made using the SCAN [25-26]. It is a semi-structured standardized clinical interview. Rating is done on the basis of matching the answers of the respondent against the definitions of the symptoms in a glossary, which is an integral part of the instrument. The interviewer is trained to rate the presence and degree of severity of symptoms independent of their relevance to any possible diagnoses that may or may not eventually apply to the subject being interviewed. The SCAN

provides a diagnosis compatible with the DSM IV and International Classification of Diseases (ICD 10). A diagnosis of MDD was made when a stroke survivor had at least five symptoms of depression occurring persistently for two weeks or more. These symptoms must include either depressed mood or anhedonia, or both [21]. Training for the SCAN was achieved at the University of Ibadan, a WHO recognized training centre.

Cognitive assessment

Cognitive assessment was done using both the modified Indiana University Token test (Token test) [27] and the modified Mini Mental State Examination (MMSE) [28]. For the purpose of this study, the MMSE was chosen as a measure of global cognitive dysfunction, while the Token test was selected as a measure of executive dysfunction. Lower scores on these indices of cognitive functions indicate worse performance. Normative data had been established for elderly Yoruba Nigerians who were subjects in the Ibadan- Indiannapolis dementia project, a large scale longitudinal, prospective community based study of dementia in Ibadan and Indiannapolis [29]

Neuro- imaging.

The neuro-radiological characteristics of the stroke lesions were documented using CT or MRI scan techniques.

The test procedure

All questionnaires were administered by one of us, a psychiatrist. Pre and post contrast CT axial and coronal images were acquired using GE Bright speed 8 slice helical machine during the first week after the stroke. Sagittal reconstructed images were done where necessary. Non ionic (Iopamirol) contrast medium was injected intravenously before the acquisition of post contrast images. For those who had MRI scan, detailed history of metallic implants or prosthesis or other non MRI compatible objects in the patient's body were obtained. MRI was performed using Siemens Magnetom Concerto 0.2T machine. Pre contrast axial, sagittal and coronal images were acquired using T1, T2 and Fluid attenuation recovery sequences, while axial, and sagittal post contrast images using Gadolinium were acquired using T1 sèquence. The acquired CT and MRI images were reported by a consultant radiologist. In this study, hemispheric lateralization was determined by the side of the cerebral hemisphere where the lesion was located on CT or MRI scans. Also, cortical lesions were defined as damage to the cortex without involvement of the basal ganglia, thalamus, and internal capsule; and sub-cortical lesions were defined as non- involvement of the cerebral cortex. This definition is similar to those used in some previous studies [30]. Furthermore, an anterior lesions was defined as a lesion anterior to the occipital lobe, all other lesions were defined as posterior, except where they involve the cerebellum. All patients with predominantly cerebella lesions were exluded from the analyses.

Data management and analysis

Descriptive statistics were calculated for all variables. For continuous variables, means, ranges, and standard deviations were calculated. Descriptive statistics for categorical variables included proportions for binary data and the number and frequency in each category. Chi^2 was used to test the difference between groups. Student t-test was used to find the difference between means. Logistic regression analysis was done to determine odd ratios and 95% confidence intervals. Values of $p<0.05$ were considered statistically significant. Data was analyzed using the Statistical Package for the Social Sciences version 15.0 [31]

Results

Demographic and Clinical Characteristics of Subjects.

Table 1 describes the characteristics of subjects in the sample. There were 19 males (63.3%) and 11 females (36.7%) in the study sample. The mean age was 57.7 (± 9.5) years. Male survivors were older with a mean age of 58.4 (SD 11.0) years, while the mean age of female survivors was 56.6 (SD 6.3) years (table 1). In all, 27 (90%) survivors had up to 6 years of formal education. Primary school education lasts for 6 years in Nigeria and this is expected to make one literate.

Stroke was verified by CT scan in 28 (93.3%) of the study sample and by MRI scan in 2 (6.7%). Three out of every five (60.0%) stroke lesions were Infarcts. Haemorrhagic lesions were seen in 9 (30.0%) survivors. The remaining 3 had haemorrhagic infarcts (table 1). The stroke lesions were fifteen (50.0%) to the right and 15 (50.0%) to the left. Three out of every five survivors had cortical lesions while just over a quarter of the survivors (26.7%) had anterior lesions. Seven (23.3%) stroke survivors had poor MMSE, while 23 (76.7%) had poor token test scores (table 1).

Table 1: The characteristics of subjects.

Characteristics	Number	Percentage
Age (years)		
mean (± SD)	57.7 (± 9.5)	
Gender		
Male	19	63.3
Females	11	36.7
Formal Education		
0 years	3	10.0
>=6 years	27	90.0
Hemispheric Lateralisation		
Right	15	50.0
Left	15	50.0
Type of lesion		
Cerebral Infarction	18	60.0
Parenchymal Haemorrhage	9	30.0
Haemorrhagic infarcts	3	10.0
Lesion Location		
Anterior	8	26.7
Posterior	22	73.3
Cortical	19	63.3
Sub-cortical	11	36.7
Major depressive disorder	9	30.0
Cognitive Dysfunction		
MMSE (Mean ± SD)	23.9 (± 6.34)	
Dysfunction	7	23.3
Token Test (Mean ± SD)	13.0 (± 4.49)	
Dysfunction	23	76.7

Frequency of major depression

Nine (30.0 %) stroke survivors met DSM-IV diagnosis of MDD while the remaining 21 (70.0%) had no categorical diagnosis of depression (table 1).

Poststroke depression and Lesion Location.

Table 2 shows the comparison of demographic and clinical characteristics in stroke survivors in the MDD group and the non- depressed group. There were significantly more females than males among survivors with MDD (p=0.04) (table 2). There were no significant differences in the age or level of education of the MDD and the non-depressed survivors. The relationship between MDD and cognitive dysfunction by MMSE or Token test was also not significant (table 2). Similarly, hemispheric lateralisation, as well as intra-hemispheric lesion location (i.e, cortical/ subcortical or anterior/ posterior axis) had no significant relationship with MDD (p=0.47, p=0.37, p=0.13 respectively) (table 2). However, the differences in the MDD and non-depressed survivors in the type of lesions seen approached the set level of significance (p=0.06) (table 2). Logistic regression model fitted to the data showed that female gender was strongly associated

Table 2: Relationship between the characteristics and depression diagnosis

Characteristics	MDD N	%	Non-depressed N	%	X^2	O.R (95% C.I)
Age groups						
>58 yearsd	6	66.7	13	61.9	0.06	1.0 (-)
≤58 years	3	33.3	8	38.1		0.9 (0.4-2.1)
Gender						
Male	3	33.3	16	79.2	4.98*	1.0 (-)
Female	6	66.7	5	23.8		6.4 (1.2-35.4)
Education						
None	1	11.1	2	9.52	0.02	1.0(-)
Formal	8	88.9	19	90.5		0.8 (0.1-10.7)
Hemispheric lateralization						
Right	4	44.4	11	52.4	0.16	1.0 (-)
Left	5	55.6	10	47.6		1.4 (0.3-6.6)
Lesion type						
Subarachnoid haemorrhage	4	44.4	5	23.8	4.38	1.0(-)
Cerebral infarction	3	33.3	15	71.4		0.4 (0.0-6.2)
Haemorrhagic infarct	2	22.2	1	4.76		0.1 (0.0-1.5)
Lesion location I						
Cortical	4	44.4	15	71.4	1.98	1.0 (-)
Sub-cortical	5	55.6	6	28.6		3.1 (0.6-15.8)
Lesion location II						
Anterior	1	11.1	7	33.3	1.59	1.0 (-)
Posterior	8	88.9	14	66.7		4.0 (0.4-38.7)
Cognitive dysfunction						
MMSE	4	44.4	3	14.3	3.20	4.8 (0.8-28.9)
Token test	8	88.9	15	71.4	1.07	3.2 (0.3-31.55

*=p<0.05

with MDD (O.R=6.4., 95% C.I=1.16-35.44), but not lesion characteristics (O.R=0.4, 95% C.I=0.0-6.2, haemorrhagic lesions, and O.R=0.1, 95% C.I= 0.0-1.5 haemorrhagic infarcts) (table 2).

Discussion

This study measured the relationship between the types and location of stroke lesions and MDD diagnosis. Neuro-imaging facilities are available only in a small number of centres in the country setting of this study. They are also economically accessible to only a few patients. In the centres where the machines are available, they breakdown frequently because of technical problems. Our study was therefore limited to a convenience sample of 30 survivors. We report that in this small sample, most of the MDD survivors were females. Female gender was also strongly associated with a diagnosis of MDD. We could not replicate studies that have found stroke type or lesion characteristic as predictors of depression [10-15]. This may be because our sample size was too small to detect meaningful differences even if they existed. In addition, our study assessed depression using a rather restrictive but more rigorous evidence based DSM system [21-32]. Many of the previous clinico-pathological correlation studies have measured depression symptoms using rating scales or depression inventories with arbitrary cut-off points. Even though the sample size from which we are reporting may lack the power to detect differences in the stroke characteristics between the MDD and the non-depressed group, it detected the known gender difference in the rate of depression after stroke [33-34]. This difference is also seen in idiopathic depression [11]. We therefore postulate that large differences in lesion characteristics in the depressed and non-depressed survivors could have been detected in the same way as the gender differences if they truly existed. Perhaps a large probability sample may clarify the relationship between lesion characteristics and post-stroke major depression. Many previous studies done in the West, as well as systematic reviews of the literature have not consistently found this association [6,16-17].

Even if the site and size of the brain lesion after stroke were significantly correlated with depression, it would remain difficult to conclude that this is the only reason why survivors become depressed. For instance, the relative loss of independence in the performance of instrumental or basic activities of daily living subsequent to the stroke event, as well as the feeling of helplessness that may result from such disability may independently predispose the survivor to depression [4]. Although it is still not clear if certain types or degrees of neurological impairment and disability are associated with more depression or less of it [35].

Similarly, it is difficult to discard the influence of certain neuro-physiological changes such as stress induced changes in the hypothalamo-pituitary-adrenal (HPA) axis and cortisol levels which are also known to be present in the causal pathway to depression [36]. It would therefore appear that there may be other non stroke related factors inherent in the survivors or their social environment predisposing them to depression after stroke. The finding in this study that female gender was predictive of MDD and not any of the lesion characteristics is further supportive. Also in line with such psycho-social model for post-stroke depression is the proposition by some authors that the survivor's affective reserve is diminished by a stroke, thereby uncovering underlying vulnerabilities for depression [37]. This may also explain why in some studies the lesion characteristics as well as other biological variables are associated with depression, and in other studies this associations are not demonstrated.

In interpreting our results, it is important to consider some of the limitations: the analysis was based on a small sample of convenience. This would hardly be enough for generalization. We also relied on evidence from mostly CT scans that were done in the routine clinical assessments of the survivors during the acute phase of the stroke events. This study however sets the tone for future studies of clinico-pathological correlation of stroke lesions and emotional disturbances in an under-researched African cohort. Future clinico-pathological correlation researches in Nigeria should be more specifically designed using more advanced neuro-imaging techniques, and involving a large probability sample of stroke survivors.

We conclude that stroke lesions in the acute phase of stroke could not completely explain the high prevalence of depression among survivors attending physiotherapy in Nigeria. The occurrence of depression among stroke survivors may ultimately be determined by a combination of psychosocial, historical, and other biological factors.

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