Original Article

Depression impedes neuroplasticity and quality of life after stroke

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Abstract

Background and Purpose: Depression following a stroke/poststroke depression (PSD) has been newly recognized as one of the most common complications after stroke. PSD may affect neuroplasticity and quality of life. The purpose of present study was to find out effects of depression on functional recovery, quality of life and neuroplasticity in patients with acute stroke. **Methods:** A total of 76 cases were recruited for the study and out of which 44 were available for the analysis after six months. Patients were divided into three groups according to severity of depression: Group A (without depression), Group B (mild-to-moderate depression), and Group C (severe depression) on the basis of Patient Health Questionnaire-9 (PHQ-9) scale scores. All patients were assessed for depression by PHQ-9, and for quality of life by Stroke Specific Quality of Life (SSQOL) scale. Neuroplasticity was assessed by measuring levels of serum brain-derived neurotrophic factor. **Results:** Quality of life was observed to be significantly affected by depression ($P \leq 0.05$). The most commonly affected characteristics were energy, family roles, mobility, self-care, social roles, upper extremity function, and work productivity. Serum BDNF levels were also affected significantly by depression ($P \leq 0.05$). **Conclusion:** PSD is a serious complication, affecting quality of life and neuroplasticity (BDNF) in patients. Decreased neuroplasticity further may affect functional improvement.

Keywords: BDNF, poststroke depression (PSD), neuroplasticity, quality of life, stroke

Introduction

Despite decrease in stroke mortality rate, there has been increase in the stroke survivors with residual disability and impairment. This has grown interest in the factors that can affect recovery from stroke and quality of life.[1] Depression after stroke or poststroke depression (PSD) is one of the factors that can negatively influence the functional outcome after stroke but is often ignored. With a possible role also in cognitive status and survival, it is an obvious source of suffering for patients and caregivers.[2] PSD may impede rehabilitation, recovery, quality of life, and caregiver's health.[3-6] Depression after stroke, though recognized for more than a century, had never received the attention that has been devoted to other stroke complications, such as motor impairment, language problems, or cognitive deficits.[7] PSD not only leads to poor involvement in rehabilitation and delays functional recovery but results in limited social activity and increased disability.[8,9] Moreover, 12.3–73.2% of stroke survivors suffer from concurrent depression and anxiety which further delays recovery from stroke.[10-12]

The prevalence of PSD (13.7–31.1%) is four times higher than the likelihood of having depression in the general population without comorbid physical disease. When physical recovery is the main focus of treatment, occurrence of depression and

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Received: 17-02-2020 **Revised:** 13-03-2020
Accepted: 07-04-2020 **Published:** 25-08-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_273_20

How to cite this article: Chaturvedi P, Tiwari V, Singh AK, Qavi A, Thacker AK. Depression impedes neuroplasticity and quality of life after stroke. J Family Med Prim Care 2020;9:4039-44.

anxiety can be overlooked in the early stage of stroke recovery.[8,13] Consequently, depression and anxiety are usually diagnosed poorly and inadequately treated.[8,14] Recognizing these symptoms is difficult because they often overlap with stroke-related impairments.[11,14]

Based on the literature, the most consistent factors associated with PSD are severe stroke and physical disability.[15] Close relationship between PSD and neurological deficits suggests that PSD may be a psychological, reactive depressive symptom associated with sudden functional deficits.[16,17] When there are prolonged functional deficits, subsequent familial and social issues may perpetuate PSD.[18] Several clinical studies on major depressive disorder (MDD) have shown that blood–brain-derived neurotrophic factor (BDNF) is associated with depression response. BDNF is a neurotrophin related to neuronal survival, synaptic signaling, and synaptic consolidation.[19] Several studies have been performed assessing BDNF levels in MDD and showing important correlations between MDD and BDNF levels.[20]

Studies regarding the PSD and its impact on neuroplasticity and quality of life are still lacking. The current study was designed to assess patients for depression (by Patient Health Questionnaire-9 [PHQ-9]), levels of serum brain-derived neurotrophic factor (S. BDNF), and their impact on quality of life (by Stroke Specific Quality of Life Scale [SSQOL]) in patients with stroke.

Subjects and Methods

We prospectively collected 76 cases with stroke. Patients between 18 and 70 years of age, >3 weeks after their first stroke, and modified Rankin score between 2 and 4 were recruited for this study from the Department of Neurology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow. The study has been approved by the Institutional Ethics Committee. An approved written informed consent was obtained from each patient prior to recruitment into the study. All patients were divided into three groups on the basis of severity of depression: group A (without depression), group B (mild-to-moderate depression), and group C (severe depression) as summarized in Table 1. Patients with prestroke history of antidepressant use, any psychiatric illness, recurrent stroke, and aphasia were excluded from the study.

Analysis of BDNF concentrations: Blood was drawn, between 8 and 10 AM, and serum was separated by centrifugation and stored at − 80°C until assayed. The procedure was repeated in all the groups after one and six months of admission. BDNF levels were measured through enzyme linked immunosorbent assay (ELISA), using the commercially available kit (Ray Biomed Human BDNF ELISA kit). Absorbances were measured at a wavelength of 450 nm.

Quality of life was assessed by SSQOL and depression was assessed by PHQ-9 scale. All assessments were done at the time of admission and repeated at one and six months after admission.

Table 1: Classification of patients on the basis of Patient Health Questionnaire-9

Groups	No. of cases	Scores (PHQ-9 scale)	Severity of depression
Group A	10	<4	No depression
Group B	16	<14	Mild-to-moderate depression
Group C	18	>15	Severe depression

The PHQ-9 performs well as a brief screener for PSD, superior to other depression measures and similar to its characteristics in a primary-care population. Moreover, PHQ-9 scores discriminate equally well between those with and without PSD regardless of age, gender, or ethnicity.[21]

Each patient received routine medical and physiotherapy management (Proprioceptive Neuromuscular Facilitation Exercises, speech therapy, and occupational therapy) to control poststroke complications. All the patients were followed up in OPD of department of Neurology on monthly basis until six months.

Statistical analysis was performed using the Statistical Package for the Social Sciences software, version 20.0. One-way ANOVA compared the demographic and clinical characteristics and difference in means at different time intervals between the three groups of patients—A, B, and C. Spearman correlation assessed correlation between PHQ-9, serum BDNF levels, and SSQOL scores. Level of significance was set at $P \leq 0.05$.

Results

Out of 76 patients recruited, 4 had recurrent stroke (5.2%), condition of 3 deteriorated (3.9%), 4 expired (5.2%), 1 underwent surgery (1.31%), 3 were aphasic (3.9%), 12 were lost to follow-up (15.7%), and blood sample of 5 (6.5%) patients was not available at 6 months. Only 44 (57.8%) patients were available for analysis with complete six months of follow-up. Patients in group A were without depression ($n = 10$; 23%), group B had patients with mild-to-moderate depression ($n = 16$; 36%), and in group C, PSD was severe ($n = 18$; 40%). There was no significant difference in age, Glasgow Coma Scale, Modified Rankin Scale, side affected, type of stroke, and days between strokes in all groups as summarized in Table 2.

There was significant difference in PHQ-9 scores in all three groups. On assessing all components of SSQOL scale, we found that family role, self-care, social role, and work productivity were significantly affected by depression ($P < 0.05$) [Table 3, Figure 1]. Energy level was affected significantly ($P < 0.05$) by depression. Depression had significant effect on mood and thinking during the hospital stay only. There was moderate negative correlation

Table 2: Demographic characteristics of patients with stroke

Variables	Scores			*P*
	Group A *n*=10	Group B *n*=16	Group C *n*=18	
Age in years (SD)	56.87±11.59	59.29±11.79	59.33±12.53	0.927
Gender (male/female)	7/3	6/10	12/7	>0.05
Side affected (right/left)	4/6	3/13	7/11	>0.05
Type of stroke (ischemic/hemorrhagic)	4/6	4/12	8/10	>0.05
Glasgow coma scale	15	15	15	0.718
Modified Rankin Scale (SD)	2.40±0.548	3.40±0.463	3.75±1.00	0.280
Days between stroke (SD)	19.07±1.84	18.18±3.04	21.00±.894	0.960
PHQ-9 scores (SD)	1.8±0.4	9.33±4.03	15.30±4.02	**<0.01****
Serum BDNF levels (ng/ml)	16.06±2.02	9.75±3.85	9.26±2.18	**<0.01****

NIHSS: National Institute of Health Stroke Scale, PHQ-9: Patient Health Questionnaire-9, S. BDNF: serum brain-derived neurotrophic factor, SD: standard deviation; level of significance at $P \leq 0.05$**

Table 3: Stroke-specific quality-of-life scale (SSQOL) affected by depression in stroke patients

	At admission				After 1 month				After 6 months			
	Group A	Group B	Group C	*P*	Group A	Group B	Group C	*P*	Group A	Group B	Group C	*P*
Energy	12.08±1.71	9.09±4.36	9.00±4.48	**0.041***	14.77±0.66	10.54±3.50	10.15±4.12	**0.003****	15.0±0.00	12.36±3.10	11.00±4.18	**0.010****
Family roles	14.11±1.36	12.09±3.01	9.42±3.18	**0.01****	14.77±0.44	13.18±2.08	11.52±2.41	**0.01****	15.0±0.00	13.0±3.09	12.89±2.15	**0.049***
Language	24.56±0.72	19.55±7.5	18.53±6.36	0.059	24.77±0.44	21.63±7.24	23.52±2.65	0.413	25.00±0.00	22.63±5.25	23.94±1.68	0.357
Mobility	24.66±7.49	18.45±7.36	14.42±9.4	**0.011****	26.66±4.74	24.63±7.04	20.21±8.38	**0.022***	29.00±1.73	26.54±4.59	23.89±7.34	**0.045***
Mood	23.86±1.69	19.73±5.36	16.95±6.91	**0.014****	24.77±0.44	20.45±6.10	20.15±6.57	0.112	24.33±1.32	22.00±6.43	21.78±4.14	0.349
Personality	11.22±3.02	11.64±4.54	11.37±4.57	0.992	11.66±3.96	12.18±4.75	11.47±4.29	0.935	12.11±3.65	12.54±4.03	13.52±1.83	0.498
Self-care	20.33±5.70	14.73±5.51	11.58±6.55	**0.006****	21.66±4.24	19.45±4.88	14.73±6.83	**0.010****	22.77±3.86	22.27±2.49	16.68±7.45	**0.009****
Social roles	20.89±3.91	12.45±5.48	9.95±5.07	**0.01****	22.77±2.72	18.27±6.35	12.05±6.52	**0.01****	23.22±2.53	21.00±4.04	15.89±6.42	**0.01****
Thinking	14.78±0.44	11.53±4.05	11.11±4.56	0.938	13.00±3.96	11.63±5.18	11.52±4.18	0.713	13.44±3.08	11.18±4.99	12.52±3.20	0.305
UE function	18.78±8.19	12.82±5.81	8.26±6.03	**0.003****	19.66±8.39	15.81±5.63	9.42±8.28	**0.007****	20.55±8.81	19.63±5.78	12.57±7.72	**0.007****
Vision	14.11±1.76	13.91±1.51	14.21±1.65	0.777	14.77±0.440	14.63±0.92	14.52±0.90	0.710	15.00±0.00	17.54±9.12	14.78±0.53	0.475
Work productivity	10.33±3.70	6.18±3.97	4.42±1.98	**0.01****	11.22±3.56	6.36±3.82	5.84±3.21	**0.001****	13.00±2.95	7.90±4.30	7.31±4.61	**0.008****

UE: Upper extremity; Level of significance at $P \leq 0.05$*; $P < 0.01$**

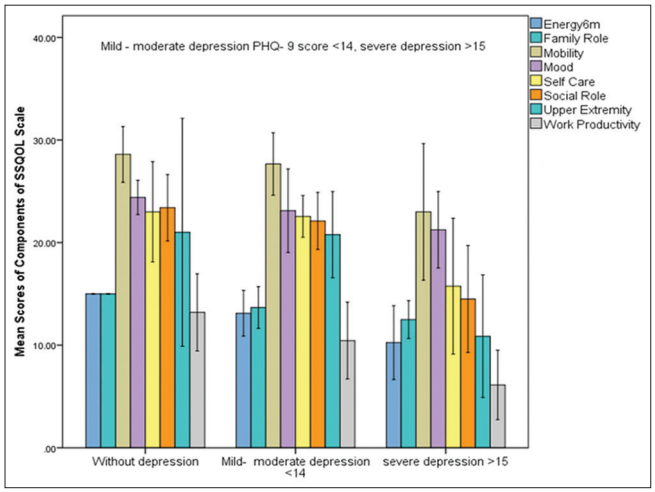

Figure 1: Components of SSQOL scale affected by depression

between PHQ-9, serum BDNF, and quality of life (SSQOL scores) [Table 4]. Better improvement in serum BDNF levels and quality of life [Figure 2] from admission to six months was seen in patients without depression and mild-to-moderate depression but there was a decline in BDNF level in the group with severe depression. A higher overall SSQOL score is observed in patients without depression in comparison to patients with depression, as depicted in Figure 3.

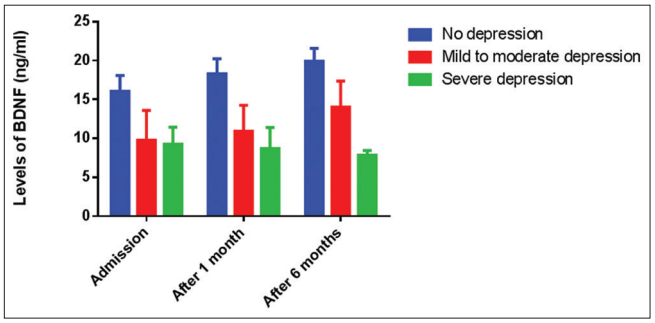

Figure 2: Levels of BDNF in patients without, mild-to-moderate and severe depression

Discussion

Besides disability, quality of life after stroke is affected by a variety of other factors. According to previous researches, functional disability is most frequently associated with PSD as a psychological reaction to physical impairment. There are findings that orthopedic patients with comparable disability are less frequently depressed than patients of stroke are.[22] The main aim of our study is to observe the possible causes of depression after stroke and its impact on quality of life. One possible cause may be reduced levels of BDNF in serum. In our study, we found that patients with mild depression exhibited improvement in serum

Table 4: Correlation between PHQ-9 scores with Serum BDNF levels and SSQOL scale scores

	(PHQ-9) scores	
	r^2 S. BDNF	*P*
At admission	−0.164	0.066
After 1 month	−0.287	**0.001****
After 6 months	−0.755	**0.001****
	SSQOL scale	
At admission	−0.112	0.155
After 1 month	−0.132	0.092
After 6 months	−0.234	**0.003****

S. BDNF: Serum brain-derived neurotrophic factor, SSQOL: Stroke Specific Quality of Life, PHQ-9: Patient Health Questionnaire-9; level of significance at $P \leq 0.05$**

BDNF levels and quality-of-life scores as compared to patients with severe depression. The most affected factors were energy, family role, mobility, social role, upper extremity function, and work productivity in all groups ($P < 0.05$).

Most studies have shown that functional disability is significantly more severe in depressed patients as compared to nondepressed patients. In addition, some studies demonstrated the significance of disability as a predictor of PSD,[23] while some other investigations found the association between depression and impaired functional activities to be independent of the severity of cognitive impairment, social functioning, age, and education[24] and that moderate or severe disability increased the risk of PSD by about 20%.[25] However, there are inconsistent data as some studies found no association between functional activity impairment and depression severity.[26,27] In our study, the patients without depression and with mild depression expressed significant improvement in all aspects of quality-of-life scale as compared to patients with moderate-to-severe depression, which is agreement with previous studies.

While assessing all components of quality of life, we observed that depression affected energy level significantly. Our findings suggest significant variation in energy levels between the three groups of patients at admission ($F = 3.48$, $P = 0.041$), after one month ($F = 6.61$, $P = 0.003$) and again after six months of follow-up ($F = 5.16$, $P = 0.010$) [Table 3]. Our findings are in consonance with findings of Ingles *et al.*, revealing that the frequency of self-reported fatigue problems was greater in the stroke group (68%) than in the control group (36%, $P < 0.001$) and was not related to the time poststroke, stroke severity, or lesion location.[28] One cause of fatigue may be slow neural regeneration, synaptogenesis, and angiogenesis.

Another point is the family role, which was significantly affected by depression. We observed that family roles were affected even in mild depression ($P \leq 0.05$). Our findings are in line with findings by Batool *et al.* They also reported that depression after stroke affects energy, family role, thinking, and social role significantly.[29]

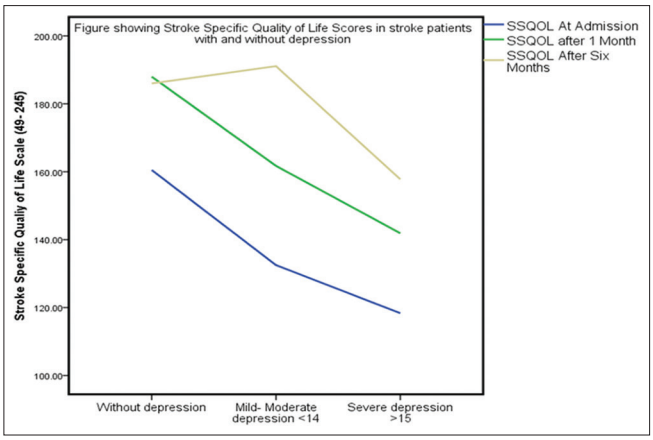

Figure 3: Stroke-Specific Quality of Life scores are decreased in stroke patients with depression

In our findings, language was not affected significantly by depression. Cognition was better in patients without depression than in patients with depression but the results were insignificant. We also inferred that depression can significantly affect mobility ($P < 0.05$). Decrease in the energy level or fatigue after stroke may be one possible cause of disinterest in activities of daily living. Lack of activity reduces serum BDNF levels that further enhance depression.

We observed that mood was affected significantly in all stroke patients at the time of admission ($P < 0.05$) but results are insignificant at one and six months. Our results show that mood is independent of depressive symptoms. Other studies have reported that mood symptoms were associated with 12- and 24-month mortality after stroke and are a grave risk factor for mortality.[30]

We observed that self-care and social roles are also significantly affected by the severity of depression. Disability after stroke results in lack of communication of the patient with the surroundings. We found that even mild depression could affect social role function. High level of family support—both instrumental and emotional—is associated with progressive improvement of functional status, mainly in severely impaired patients.

Thinking was not significantly altered by the depression. In our study, we observed that patients with moderate-to-severe stroke had difficulty in concentration, reading newspaper and thinking. However, in relation to depression, the results are insignificant.

Upper extremity function and work productivity were found to be affected significantly in all stroke survivors whether without depression, with moderate or severe depression. Although the upper extremity function is impaired due to stroke but the recovery is delayed in patients with lower serum BDNF levels. Low serum BDNF levels may cause low motor learning. Motor learning after stroke depends on the neurogenesis, angiogenesis, and synaptogenesis.

Previous studies have noticed marked rise in BDNF levels after antidepressant treatment and marked improvement in depression symptoms.[20] We observed correlation between depression and serum BDNF levels, which were significantly affected in depression, whether mild, moderate, or severe. We also observed a significant rise in serum BDNF levels in mild and moderate stroke from admission to six months, but in severe depression, the levels did not show rise.

The results of study depict that serum BDNF levels are not only associated with depression but also affect quality of life of the patient. So, every patient should be evaluated for depressive symptoms after stroke and should be given appropriate medical management. Rise in the BDNF levels improves functional outcome and quality of life.[31] Another method for increasing the levels of BDNF is prescribing the exercise to the patient from the first day after stroke. Exercises increase BDNF levels in the serum. Giving regular exercises will further prevent mortality, disability, contractures, and will help in improving the quality of life.

Conclusion

BDNF levels are associated with depression. There is decline in the BDNF levels with increase in the severity of depression. Decrease in BDNF levels further reduces chances of better neuroplasticity. So, every patient should be screened for the depression and medical management should be given.

Acknowledgment

The study was funded by Department of Science and Technology (DST), India.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Department of Science and Technology, New Delhi, India. Grant no. SR/WOS-A/LS-410/2013.

Conflicts of interest

There are no conflicts of interest.

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