



Depression, the most frequent neuropsychological problem after stroke, is greatly influenced by the complex relationships between the neurobiological and psychological changes that occur after stroke. Post-stroke depression leads to negative rehabilitation outcomes including less participation in therapy, extended recovery time, significantly decreased quality of life, and increased utilization of health care resources. Because of the high prevalence of post-stroke depression, all stroke survivors should be screened early in the rehabilitation process. Use of a biopsychosocial framework acknowledges the multifactorial etiology of post-stroke depression and contributes to effective, evidence-based treatment. Attention to the needs of the family caregivers further promotes successful post-stroke rehabilitation.

Key words: stroke, depression, risk factors, recovery, treatment

Post-Stroke Depression: Focus on Diagnosis and Management during Stroke Rehabilitation

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Introduction

The encouraging trend toward more individuals surviving stroke creates concern about how these survivors live with the residual effects. Depression, the most frequent neuropsychological problem after stroke, is estimated to affect 25–75% of survivors at some point in the months following stroke.^{1,2} The negative outcomes associated with post-stroke depression (PSD) make recognition and treatment an important aspect of the care for stroke survivors. Depressive symptoms result in less participation in rehabilitation, extended recovery time, and significantly decreased quality of life, even among stroke survivors with minor neurological deficits.^{1,3} Furthermore, PSD independently increases the risk of post-stroke mortality and is associated with increased utilization of health care.⁴ Although the etiology of PSD is complex and multifactorial, improvements in the diagnosis and treatment of this common problem may be accomplished through interventions using a biopsychosocial framework.^{1,5}

Prevalence of Post-Stroke Depression

The prevalence of PSD varies widely; depends on when depressive symptoms are measured after the stroke; whether

acute care, rehabilitation, or community-dwelling survivors are of interest; and which diagnostic criteria are used.^{6,7} In a review of 14 studies describing the occurrence of major depressive disorder (MDD) in stroke survivors, the prevalence of MDD varied widely across time. Prevalence rates peaked in the first months post-stroke, ranging between 9–37%, falling to between 5–16% at 1 year, and increasing again to a rate of 19–21% at 2 years.⁵ For a large percentage of stroke survivors who experience depressive symptoms in the early post-stroke period, there is a concern that the symptoms will become chronic. In an 18-month study, Berg *et al.*⁸ found that 46% of stroke survivors in their sample who experienced depressive symptoms at 2 months continued to have symptoms beyond 12 months. This finding is consistent with other studies in which up to half of stroke survivors, who developed MDD within the first 7–12 weeks post-stroke, had lower rates of spontaneous recovery from depression.⁵

Impact of Post-Stroke Depression

Post-stroke depression, a problem that is frequently untreated, is linked to negative outcomes for stroke survivors.^{1,2} Functional outcomes are affected not only in the

Table 1: PHQ-9 Depression Severity Scale

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✓" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

(For office coding: Total Score _____ = ____ + ____ + ____)

If you checked off **any** problems, how **difficult** have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all <input type="checkbox"/>	Somewhat difficult <input type="checkbox"/>	Very difficult <input type="checkbox"/>	Extremely difficult <input type="checkbox"/>
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Source: From the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MD PHQ). PRIME-MD® is a trademark of Pfizer Inc. Copyright© 1999 Pfizer Inc. All rights reserved. Reproduced with permission.

immediate rehabilitation period, but also over the long term.⁷ In one small sample (n = 55), remission of PSD in the first 3 to 6 months post-stroke was associated with significantly greater recovery of activities of daily living (ADL) function.⁹ However, in a larger study (n = 276), depression at 3 months post-stroke was significantly associated with poor functional outcome at 15 months (p < 0.0001).¹⁰ Quality of life was reported to be significantly (p < 0.01) lower among stroke survivors with PSD at 3, 6, and 12 months post-stroke than among survivors without PSD and even among those with significantly (p < 0.01) improved neurological status and limited disability.³ Furthermore, PSD has been associated

with increased mortality;⁷ it was found to independently increase the risk of death by 13% over a 3-year period among American military veterans.⁴ This increased risk of death appeared early in the rehabilitation period and continued over time. Finally, as in other groups of patients with depression, stroke survivors with PSD have significantly (p < 0.0001) more hospitalizations with longer lengths of stay and more outpatient visits than stroke survivors without PSD.^{2,11}

Diagnosing Post-Stroke Depression Definition

There is ongoing debate as to whether

PSD is a separate diagnosis associated with a specific neurological insult or a variation of endogenous depression. However, PSD can be simply defined as any depression occurring after stroke.² Methodological differences among PSD studies related to time since stroke, diagnostic criteria, selection bias, and research design complicate the attempts to standardize a definition.² During the immediate post-stroke period, a definition based on diagnostic criteria may be helpful in differentiating PSD from a more generalized response to situational stress. Use of criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) has been recommended in

the literature.^{2,7} Although physical symptoms of depression, as specified in the DSM-IV criteria, overlap with common post-stroke symptoms such as fatigue, decreased appetite, and sleep disturbances, evidence suggests that the use of DSM-IV criteria for depression does not lead to either over- or under-diagnosis.^{1,2,7}

Two conflicting hypotheses dominate the literature concerning the etiology of PSD.¹² The first is that PSD is primarily neurobiological in nature and is associated with the location and extent of the neurological insult.¹³ The second is the opposite; PSD is seen primarily as an endogenous psychological response to psychosocial stressors associated with stroke impairment.⁶ However, given the complex and inseparable characteristics of physical and psychiatric illness, Whyte and Mulsant⁵ suggest that the debate between the two hypotheses is unreasonable. Instead, they suggest a biopsychosocial model in which underlying vulnerabilities toward depression are exposed as the neurological and psychosocial effects of stroke decrease an individual's affective reserve. This model proposes that, much like depression in the general population, PSD develops from complex relationships between neurobiological and psychological factors and should be considered in the same manner.⁵

Evidence from the literature also suggests that perhaps PSD and depression in the general population are more similar than originally thought.⁶ A meta-analysis of 48 studies found no support for the hypothesis that the risk for PSD is related to the location of the lesion.¹⁴ Any association between lesion location and depression has been reported to disappear over the first months post-stroke.¹² In a large study ($n = 3,371$) of community-dwelling American adults over the age of 65 years, no relationships were found between MRI-identified infarctions and depression scores after controlling for age, gender, and stroke history in multiple regression analyses.¹⁵ Rather, the authors concluded, the causal pathway for depressive symptoms may be related

to the functional consequences of cerebrovascular disease. In one comparison study, no differences were found between depression that occurred following myocardial infarction and depression that occurred after stroke when controlling for age, sex, and level of functional activity limitation.¹⁶ In addition, individuals with PSD did not experience more depression symptoms, although the physical symptoms of depression were more severe compared with depressed older adults without history of stroke.²

Risk Factors for Post-Stroke Depression

Methodological inconsistencies and limitations in study design make it difficult to clearly identify those stroke survivors who may be at higher risk for developing depressive symptoms.¹⁷ Acknowledging this difficulty, Whyte and Mulsant⁵ identified common risk factors in a systematic review of English language papers. Biopsychosocial risk factors linked with PSD included history of major depression, disability, stressful life events, poor social support, and time since stroke. Recent prospective, multisite studies present the possibility of quantifying PSD risk,¹⁷ but a clinically useful model remains elusive.¹⁸ The multicentre DESTRO study attempted to identify and quantify risk factors for PSD in a large sample ($n = 1,064$) of stroke survivors.¹⁷ During the study period 36% of the sample developed PSD primarily in the first 3 months post-stroke. The majority of survivors with PSD (81%) were diagnosed with dysthymia using DSM-IV criteria. Consistent with the literature, disability and previous depressive episodes were found to place survivors at an increased risk of PSD. Additional risk factors included female sex, previous psychiatric disorders, and previous cerebrovascular episodes. Combinations of these factors exponentially increased the risk for PSD. The Auckland Regional Community Stroke (ARCOS) study followed 739 stroke survivors to determine clinically useful predictors of abnormal mood after stroke.¹⁸ After controlling for age, sex, and comorbidity in a multi-

variate logistic regression analysis, disability and history of depression were identified as key baseline predictors of abnormal mood at 6 months post-stroke. However, a lack of clinically meaningful predictive ability limits the usefulness of this model.¹⁸ The findings from the above literature review and studies emphasize the multifactorial nature of PSD and the need to consider biopsychosocial risk factors similar to other types of depression.

Screening for Symptoms

Because PSD can negatively affect rehabilitation outcomes, all stroke survivors should be actively screened for depressive symptoms during the rehabilitation period.¹ A number of standardized screening tools are available; however, it is important to consider the purpose of various tools and whether the tool has been validated in the stroke population. The Center for Epidemiology Studies – Depression (CES-D) and the Beck Depression Inventory (BDI) are commonly used for screening purposes in this population. However, a tool that is designed to diagnose and monitor response to treatment may be more useful in the clinical setting.^{2,7} The Patient Health Questionnaire (PHQ)-9 Depression Severity Scale (shown in Table 1) is shorter than other tools, can be used to screen for and diagnose depression, is sensitive to change, and has been validated in the stroke population.¹⁹ Based on the nine DSM-IV depression symptoms, the PHQ-9 is also able to discriminate between stroke survivors with and without PSD regardless of age, sex, or ethnicity.

Treatment of Post-Stroke Depression

Pharmacological, psychotherapeutic, and caregiver/social support interventions should all be considered in an effort to stabilize mood, improve participation in therapy, and improve rehabilitation outcomes because of the multifactorial nature of PSD.¹ Recent improvements in functional neuroimaging and neurophysiological techniques suggest that recovery from stroke may be potentiated by

Key points

Due to the high prevalence rate and related negative outcomes, all stroke survivors should be screened for post-stroke depression (PSD) during rehabilitation.

The etiology of PSD is multifactorial with both neurobiological and psychosocial causes.

Risk factors for PSD include, but are not limited to, level of post-stroke disability, history of depression, female sex, and poor social support.

Treatment for PSD is similar to treatment for non-stroke-related depression.

Treatment should be directed by evidence-based guidelines, including pharmacological, psychotherapeutic, social support, and caregiver support interventions.

both pharmacological and behavioural interventions that lead to dynamic changes in the brain after stroke.²⁰ There is moderate evidence that interventions to improve social support for caregivers also can improve the rehabilitation outcomes of stroke survivors.²¹ Furthermore, caregivers are often able to provide information about PSD symptoms that stroke survivors may be reluctant to discuss with their health care providers, thereby reducing a potential barrier to treatment.²²

Pharmacological Treatment

Selective serotonin reuptake inhibitors (SSRI) and tricyclic antidepressants (TCA) have been the most frequently studied antidepressants.¹ Post-stroke depression is reported to be responsive to either SSRI or TCA, with up to 60% of stroke survivors responding to these medications.⁵ Using SSRI medications may be preferred for older adults who have experienced stroke because the side effect profile is more favourable. Typically SSRIs have fewer cardiotoxic or anticholinergic side effects than TCAs and are less likely to cause sedation.^{1,6} There is a lack of evidence to support the routine prophylactic use of antidepressants; therefore, this practice is not recommended by clinical practice guidelines.¹

Although PSD symptoms respond to medication, questions arise as to the effect of pharmacotherapy on depression remission rates and on rehabilitation outcomes. A recent review of seven random-

ized or quasi-randomized placebo-controlled trials concluded that, although antidepressant treatment reduces symptoms, there is no clear effect on remission of depression and no evidence that antidepressant treatment improves functional recovery.²³ However, the studies in this review were limited in that the duration of treatment was shorter than that recommended by the American College of Physicians guidelines, there was wide variability in diagnostic criteria, and the time between stroke onset and enrollment in the trials also varied widely.²³ Similarly, Cassidy and colleagues²⁴ concluded that depression severity was not a significant predictor of rehabilitation effectiveness as measured by functional outcomes and that the relationship between depression and rehabilitation outcomes may have been masked by treatment received by 6 of the 10 participants who were diagnosed with major depressive disorder. Furthermore, with the small sample size, there was insufficient power to determine the effect of depression on functional outcomes. Additional research is needed to clarify these relationships.

Care management and monitoring of antidepressant therapy may answer questions about the effectiveness of antidepressant medications in reducing and alleviating the symptoms of PSD. In one study²⁵ using an activate-initiate-monitor model (AIM), care managers monitored the effectiveness of antidepressant medications and adherence to the treat-

ment protocol. Medication dosages and classes were changed as indicated by patient response using a pre-established algorithm. Positive depression response (51% vs. 30%, $p = 0.005$) and remission (39% vs. 23%, $p = 0.01$) were both more likely in the AIM group than in the usual care group. A difference in response was noted by the 6-week assessment and continued through 12 weeks. Importantly, this study demonstrates that following evidence-based guidelines for depression treatment is associated with significant improvement in the remission of depression. Furthermore, the study findings support the concept that PSD should be treated similarly to non-stroke-related depression.²⁵

Psychotherapeutic Interventions

The evidence for psychotherapeutic interventions in the reduction and remission of PSD symptoms is not as strong as for treatment with antidepressive medication. However, clinical guidelines report some evidence for the effectiveness of cognitive-behavioural therapy in conjunction with antidepressant medication. Brief supportive therapy is recommended.¹ Cognitive-behavioural therapy alone shows some promise.⁶

Social Support Systems

Support of the caregiver is an emerging aspect of stroke rehabilitation.²⁰ Clinical guidelines state that adequate support of stroke survivors by their family caregivers and other family members is critical to successful rehabilitation outcomes.^{1,21} However, the levels of psychological distress and morbidity experienced by caregivers are of great concern and may limit the amount of available support. Canadian evidence-based practice standards recommend that stroke survivors and their caregivers receive physical help, respite care, and emotional and educational counseling.²¹ Training of caregivers has been reported to reduce overall costs associated with stroke recovery and, in one study, resulted in improved psychological outcomes and quality of life for stroke survivors.²⁰

Conclusion

Despite the heterogeneity of the literature on identifying and treating PSD, some conclusions may be drawn about the appropriate care of stroke survivors experiencing PSD. First, a biopsychosocial approach to treatment will address both the physiological and psychological aspects of depression after stroke. All stroke survivors should be screened during rehabilitation in the first weeks to months post-stroke because of the high prevalence of PSD. Patients who have a positive screen for PSD should be followed with a tool that is sensitive to change over time and should receive evidence-based treatment including pharmacological, psychotherapeutic, and social support interventions along with support for their family caregivers. Early detection and treatment of PSD may improve functional outcomes and quality of life while also reducing the overall cost of care.



No competing financial interests declared.

Acknowledgements

Portions of this manuscript were supported by the following sources: NIH/NINR grants F31 NR010156 (PI Johnson) and K01 NR008712 (PI Bakas), and the IUPUI Graduate Office Research Incentive Funds Program (Johnson). Phyllis Dexter, RN, PhD is acknowledged for her editorial assistance.

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