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Evaluation & Treatment of Psychological Effects of Stroke

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Abstract

Strokes are a common medical condition in the United States, including in Delaware. An under-recognized effect of stroke is the impact on mood that often occurs. Many individuals develop depression, anxiety, PTSD, and other psychological sequelae. These disorders can significantly affect their lives and their relationships. The emotional effects of stroke pose a public health problem for our residents, leading to devastating decreases in the quality of life for the patient and the family. These challenges negatively impact the community due to the associated healthcare and economic burdens. The population of the State of Delaware is growing, and the proportion of senior residents, who are also at greater risk for strokes, is also increasing. Strokes will remain an ongoing important clinical concern for our healthcare providers. Emotional changes after a stroke will occur in many Delaware residents who suffer a stroke. The emotional sequelae of stroke are under-treated. It is critical for healthcare professionals to be trained to recognize, assess, and treat the psychological disorders that can result from having a stroke. This article provides an overview of the major psychological effects of stroke, recommended assessment tools, promising treatment trends, and directions for further research. Improving our ability to detect and treat these difficult emotional challenges can facilitate effective treatment and prevention strategies and increase quality of life for stroke survivors, their loved ones, and their communities.

Introduction

Strokes are unfortunately common across the world. Approximately 12.2 million new strokes occur globally per year.[1] In the United States, an estimated 795,000 people suffer a stroke annually.[2] In the state of Delaware, 3,139 strokes were recorded in 2022.[3] Delaware's population was estimated at 1,018,392 in mid-2022[4]; this suggests that the state's per capita rate of strokes was about 0.31%.

Survivors of stroke face enormous health, emotional, social, and economic impacts. These effects are experienced at the personal, family, and community levels. Significant complications of stroke include the psychological ramifications that often develop. Post-stroke mood disorders are prevalent yet tend to be under-recognized and under-treated. This clinical challenge was brought to the public's eye when earlier this year a U.S. senator from our neighboring state of Pennsylvania, John Fetterman, sought hospitalization for his post-stroke depression. He also had a prior history of depression.

Mood disorders apart from stroke are also common around the globe. Approximately 280 million people worldwide live with depression.[5] In the United States, it is estimated that 21 million adults aged 18 or older have experienced depression, which is about 8.4% of the adult population.[6] One study indicated that, according to standard diagnostic criteria, the twelve-month and lifetime prevalence of major depressive disorder are 10.4% and 20.6% respectively.[7]

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Not surprisingly, stroke is one of the most disabling medical conditions in the US.[8] Marked changes in functional and psychosocial functioning are not only experienced by patients with stroke. Psychiatric disorders can lead to disabling conditions as well. Depression is the leading cause of disability in the United States.[9] When stroke and mood disorders are co-occurring, they often generate significant personal and public health consequences. Numerous studies over the past few decades have indicated that post-stroke psychological sequelae can be varied as well as pervasive.[10,11] Psychological effects of stroke include depression, anxiety, post-traumatic stress disorder (PTSD), mania, psychosis, irritability, and apathy, among other emotional and behavioral conditions.[12] This review will focus on the first three more commonly observed post-stroke psychological sequelae.

Post Stroke Depression

The most thoroughly researched emotional issue following stroke is depression (PSD). A large body of studies over several decades indicates that roughly 1/3 of individuals sustaining a stroke develop PSD within a year to five years post-onset.[13] These individuals have higher rates of healthcare utilization, poorer functional outcomes, reduced quality of life (QOL), and higher mortality.[14,15] The depression these patients suffer is not simply due to having a serious medical condition; for example, when compared with patients suffering myocardial infarctions, those with PSD experience higher rates of mood disorders, particularly depression.[16,17] While the one-third prevalence rate for PSD is well-supported across studies, some studies have reported lower rates ranging from 15.8% to 21%, depending on setting and time since stroke.[18,19] Higher rates have also been reported, and the cumulative incidence of PSD may be as high as 55%.[20] The varying rates of depression after stroke are due to combined factors, mostly related to methodology. For example, there is a lack of standardization of assessment instruments, leading to inconsistent criteria and cut-off scores. Subject inclusion and exclusion criteria are also variable such that “minor depression” and depressive adjustment disorders may or may not be included in investigations of stroke patients with depression, and aphasics and patients with hemorrhagic strokes are often excluded. Time points of assessments relative to stroke onset vary as well. Additionally, geographic region influences the selection and assessment processes. These are only a sampling of the factors that contribute to the variability in the incidence and prevalence of PSD reported across studies. Despite these limitations, it is evident that depression is more common after stroke than its incidence in the general population.[10] Understanding the risk factors may assist in optimizing clinical assessment, honing treatments, and developing prevention strategies.

Risk Factors

Post-stroke depression is a multifactorial condition.[21] There are combined psychological, social, and biological factors that play a role in its manifestation.[22] Identification of risk factors is an important area of study for clinical work. The research heterogeneity noted earlier for diagnostic considerations applies to our understanding of risk factors for PSD as well. The variations in research design lead to issues concerning methodology, selection criteria, population setting, geographic location, assessment tools, cut-off scores, time since stroke, etcetera. These irregularities cause difficulty in identifying a clear and consistent set of predictors of PSD across studies. Despite this ambiguity, there are some PSD predictors that warrant comment and further study. These risk factors include (though are not limited to) the following:

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Genetic

Studies suggest that there are many genes associated with post-stroke depression.[21,23,24] These genes include the serotonin transporter gene (SERT) polymorphisms, 5-HTTLPR and ST*in*2 VNTR.[21] Apolipoprotein E (ApoE) and methylenetetrahydrofolate reductase (MTHFR) appear to be associated with a higher risk of major depressive disorder following a stroke, and research continues into the identification of genetic contributions to risk for post-stroke depression.

Age

A systematic review, which included 23 studies and 18,374 participants, found that most studies concluded that older age was not associated with an increased risk of depression following a stroke.[21] One review indicated that age of stroke at less than 70 years was predictive of PSD, but limited sample size was a drawback.[25] Given the mixed research findings, age remains an ambiguous risk factor.

Sex

Research across the decades has yielded mixed results in relation to gender and susceptibility for post-stroke depression.[21] A large body of evidence had suggested that females were more likely to develop depression post-stroke than males.[16,25] There are also some research findings casting doubt that a specific gender increases the risk of depression following a stroke.[22,26]

Stroke Severity

A number of studies have demonstrated that the severity of stroke is positively correlated with depression.[21,27] However, a recent review indicated that stroke severity was not predictive of PSD, while level of physical disability was predictive during the first-year post-stroke.[28] These two constructs may be conflated in some cases, depending upon definition and assessment tools employed in the study samples. Stroke severity therefore may be a consideration for PSD, depending upon its definition and how it is measured.

Lesion Location

Research has demonstrated that the distance between the brain lesion and the frontal lobe plays an essential role in determining the severity of post-stroke depression.[21] More specifically, comparisons between left prefrontal-subcortical lesions (i.e., lesion volume & location) versus right hemisphere have demonstrated that individuals with left hemisphere lesions have a higher incidence and severity of post-stroke depression. Numerous studies have questioned this trend. For example, Robinson and Jorge[12] reviewed meta-analyses which did not confirm a strong association between lesion location and subsequent depression. They concluded that there may be an association of PSD with left frontal or basal ganglia lesions within two months of an initial clinical stroke. Findings from a separate review showed some support for this observation, while also indicating that both frontal and subcortical lesions regardless of laterality may be somewhat predictive of PSD.[29] At this time, the relationship between lesion location and PSD is not fully understood and may be mediated by other factors.

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Aphasia

Depression after stroke may be more likely when a patient has aphasia as compared to patients without language impairments.[19] A study of adults with aphasia in an acute care setting indicated that the aphasic patients were seven times more likely to suffer PSD than non-aphasic patients.[30]

Other Factors

Research suggests that marital status, years of education, history of prior stroke and/or history of myocardial infarction, recent life stressors, poverty, and lack of social supports are associated with a higher incidence of depression following a stroke.[18,21,31]

Assessment

The assessment of PSD across sites and studies is highly variable in terms of methods, instruments, cut-off scores, definitions of depression and types of depression, settings, and time points of assessment. For example, brief screenings may be employed, usually administered by a clinician; a lengthier structured interview adhering to DSM-5 Diagnostic and Statistical Manual of Mental Disorders[32] criteria can be conducted by a clinician; or a range of approaches in between these methods might be used for depression assessment. The methods include self-report inventories or checklists, mood scales, structured interviews, and clinician or collateral observer ratings.

The studies reviewed in the literature tend to use the following validated instruments: Hospital Anxiety and Depression Scale (HADS);[33] Center for Epidemiologic Studies of Depression Scale (CESD);[34] Hamilton Depression Rating Scale (HAMD or HDRS);[35] Patient Health Questionnaire-9 (PHQ-9);[36] Beck Depression Inventory (BDI);[37] and Geriatric Depression Scale (GDS).[38] The instruments vary in administration time requirements and staff involvement; therefore, practicality and efficiency needs may dictate instrument selection on a busy acute inpatient or rehabilitation unit.

A few reviews of assessment instruments (Table 1) employed with stroke survivors indicate that several types of methods may be useful. Clinician-administered structured clinical interviews and screening scales for depression showed acceptable or better results for all validation measures when used to screen for psychiatric disorders in patients with stroke in a review from 2016.[39] Another review suggested that the CES-D, the HDRS and the PHQ-9 may be the best options for adequate sensitivity and specificity.[40] Other studies have indicated that despite limitations, the Patient Health Questionnaire-2 (PHQ-2) may be practical for screening due to minimal time and staff demands and acceptable sensitivity.[41–43] The authors agree that ideally the instruments should not be used in isolation. A follow-up evaluation utilizing more detailed assessment is recommended, such as following a positive PHQ-2 with PHQ-9, other more focused clinical instruments, and/or direct interview.

There is a potential confound with most of these instruments, in that some of the physiological symptoms of depression overlap with those of stroke. For example, sleep quality, energy level, and appetite are often diminished in hospital patients independent of presence of mood disorder. Yet these symptoms are often altered in depression and are typically included in surveying depression. To minimize the confound, and for practical clinical goals as indicated earlier, the PHQ-2 may be preferable for depression screening purposes in hospital settings.

Many of the studies addressing screening and diagnosis of post-stroke depression excluded patients with aphasia. Assessment of depression in these patients can be particularly challenging. Communicative disorders can impact comprehension, not just expression. Reading, writing, spelling, and gesture can be compromised. Validity and reliability of the instruments may be tenuous when used with aphasic patients. The Visual Analogue Mood Scale (VAMS)[44] has been utilized to help skirt the communication issue. Its utility may be questionable in some cases. There are concerns that it has not been found to be consistently reliable,[45] while other researchers find it to be of value in assessing individuals with aphasia.[46]

Other Psychological Sequelae of Stroke

In addition to depression, there are other noteworthy psychological sequelae of stroke. Though less common and less studied, these emotional effects pose potential burdens to patients, families, and the community. Anxiety and PTSD are two of the emotional consequences that are most often observed after depression in patients with strokes.

Anxiety is relatively common following a stroke. In the general population, 19.1% are estimated to have anxiety.[47] After stroke, it is estimated that 20-25% of patients develop anxiety.[48–50] Anxiety disorders include specific phobias, generalized anxiety disorder (GAD), panic disorder, agoraphobia, and social anxiety disorder. An adjustment disorder with anxiety may also account for the observed symptoms. Anxiety due to another medical condition (other than stroke) and substance use-induced anxiety are typically ruled out and not included in populations under study in these investigations. Post-stroke anxiety (PSA) may tend to present as specific phobia with or without associated GAD.[51] PSA is closely associated with PSD and tends to endure for longer periods when the two conditions co-occur.[52,53] Pre-stroke depression, stroke severity, early anxiety, and dementia or cognitive impairment after stroke appear to be predictive of post-stroke anxiety.[54] PSA is typically assessed by the GAD-7;[55] the Beck Anxiety Inventory (BAI);[56] HADS;[33] and the Hamilton Anxiety Rating Scale (HAM-A).[57] These instruments have not been validated for stroke populations despite their use clinically and in research with this patient group.

Post-traumatic stress disorder (PTSD) has been observed in some patients following stroke. Suffering a stroke can be perceived as a disruptive and marked traumatic life event.[58] Prevalence estimates vary, generally from 10% to 31%, depending upon assessment method employed and other factors.[59] One study reported that 1 in 4 stroke survivors endorsed elevated symptoms of PTSD within the first year.[60] Of note, PTSD was removed from the Anxiety Disorders category in 2013 in the 5th edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders and placed in the "Trauma and Stressor-related Disorders" section.[61] Post-stroke PTSD (PS-PTSD) has been associated with nonadherence to medications[62]; a heightened degree of disability;[63,64] and a higher frequency of right cerebral and brainstem lesions.[65] Risk factors were not clearly specified, though there may be a greater tendency for PS-PTSD to occur in women and at younger ages.[58,63] Social support may confer protective resilience against development of PTSD.[63] Instruments used to assess PS-PTSD include the Impact of Events Scale (IES-R);[66] Primary Care-PTSD Screen (PC-PTSD);[67] PCL/PCL-5;[68,69] and clinical interview utilizing DSM-5 criteria.

Table 1. Post-Stroke Psychological Assessment Tools

Depression	DSM-5, HADS, CESD, HAMD/HDRS, PHQ-9, BDI

Anxiety	DSM-5, HADS, BAI, HAM-A
PTSD	DSM-5, IES-R, PCL/PCL-5

Pathophysiology

The pathophysiology of post-stroke mood disorders is posited to be multi-factorial. Proposed mechanisms have been discussed in the literature for post-stroke depression more so than for other psychological sequelae. The underlying mechanisms appear to involve decreased levels of monoamines, abnormal neurotrophic response, inflammatory processes, and dysfunctional regulation of hypothalamic-pituitary-adrenal axis and glutamate-mediated excitotoxicity.[70] *G*enetic factors may also interact with the pathophysiological processes.

Prevention of Post Stroke Mood Disorders

There are suggestions that multimodal therapies combined with antidepressants may mitigate against development of PSD.[21,71] Studies have been mixed in terms of identifying any specific best practice primarily due to heterogeneity of the designs, instruments, time courses and populations. There is a lack of robust evidence to support the use of specific strategies to prevent PSA and PSD.[72] There may be a role for developing more personalized strategies incorporating integrative interventions as improved studies are conducted.[71] As mentioned earlier, social support may be a protective factor in guarding against PTSD onset.[63]

Treatment

Many individuals surviving stroke are insufficiently or ineffectively treated for psychological effects.[73] Studies indicate that post-stroke depression may respond to a variety of treatments.[74,75] Treatments of PSA and PS-PTSD are less well studied thus far.

Pharmacologic interventions

The bulk of research dedicated to treating mood disturbance after stroke focuses on pharmacotherapies. Frank et al.[70] reviewed numerous studies addressing the effects of various antidepressants on PSD. They found that selective serotonin re-uptake inhibitors (SSRIs), selective norepinephrine re-uptake inhibitors (SNRIs), bupropion, and tricyclic antidepressants (TCAs) were effective in reducing depression scores compared with placebo or “treatment as usual.” Time course in some of the studies was associated with differential effectiveness of medication. The use of SSRI’s for treatment of PSD may improve recovery through neuroprotective mechanisms and taming of inflammation, among other actions.[70]

It is well-known that not all depressed patients respond to pharmacological treatments.[76] Also, despite possible therapeutic response, in some cases the side effects are not well-tolerated. For example, in the studies reviewed by Frank et al.,[70] both SSRIs and SNRIs were often found to produce uncomfortable physiological symptoms such as insomnia and sexual dysfunction. The risk of intracerebral bleeding as well as gastrointestinal bleeding appears to be increased as well.[77,78]

TCAs and Monoamine oxidase-inhibitors (MAOIs) are considered less preferred for pharmacologic treatment due to side effects such as cardiac symptoms and preferential responsivity.[70]

In general, studies have suggested that antidepressants may improve mood, but the evidence is mixed regarding whether antidepressants significantly facilitate participation in rehabilitation and improvement in activities of daily living (ADLs).[79] Not all post-stroke patients respond well to medications.[21] There is also no consensus as to the optimal pharmacologic agent, dosage, or timing of administration. For patients with PSA, a Cochrane review indicated a dearth of high-quality evidence to guide medication regimens.[80]

The limitations posed by pharmaceuticals suggest an important role for non-pharmacologic treatments. A variety of interventions have been investigated.

Non-pharmacologic treatments

Cognitive-behavioral therapy (CBT)

Psychotherapeutic interventions, particularly CBT, have been studied in the PSD population. CBT is a psychotherapeutic approach to help individuals learn how to identify and change maladaptive thought patterns that negatively influence their behavior and emotions. This therapeutic technique, whether delivered alone or in conjunction with antidepressant medication, or in group formats, appears to decrease depression as well as anxiety symptoms that can develop after stroke.[81,82] However, the evidence for CBT as a treatment for PSD may be inconclusive due to an array of qualitative and quantitative limitations inherent in the studies. Wang and colleagues[82] suggest the usefulness of high quality RCTs to address this potentially beneficial treatment.

Related to CBT are treatments that appear potentially beneficial though not yet well studied. These include problem-solving oriented therapies and motivational interviewing.[83,84] Observed results have been promising, but limited sample sizes and small effect sizes are problematic for broader application until better designed studies are undertaken.

Neuromodulation

Non-invasive brain stimulation is a relatively recent treatment modality that may improve mood. Neuromodulation techniques such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) have recently been used to treat depression in patients without neurological disorders with beneficial outcomes.[85] Recent studies with stroke patients have reportedly demonstrated positive effects.[70,86] Further research in this area seems warranted.

Non-traditional therapies

Mind-body therapies, such as meditation, yoga, and tai chi, may be promising for offering relief from emotional suffering after stroke. A review of mind-body interventions suggested a trend toward beneficial psychological outcome but was not conclusive, possibly in part due to design limitations and decreased power of the studies.[73] Zou and colleagues[87] concluded from their analysis that yoga and tai chi are effective as “add-on” treatments to improve depression, ADLs, and mobility. Most of the studies they reviewed were conducted in China. Chan and colleagues[88] found that both yoga and exercise were significantly associated with a reduction in depression symptoms over time; however, no remarkable group differences emerged. Both exercise and yoga have been associated with positive mood and possible treatment of depression in

individuals without stroke.[89,90] Further study of these interventions for patients with PSD and PSA may be worthwhile.

Other non-pharmacological therapies recently under study suggest positive trends, though more rigorous design and replications are needed.[83,86] These interventions include life review and problem-solving therapy, music therapy, and robot-assisted neurorehabilitation.

Summary

The psychological effects of stroke such as depression, anxiety and post-traumatic stress disorder are associated with decreased quality of life in many domains, which often impact interpersonal relationships and participation in the community. PSD is one of the more common and better studied complications that can have devastating consequences for the survivor, family, and other interpersonal relationships. PSD is also associated with increased risk of stroke recurrence and mortality. This unfortunate complication of stroke has implications for Delaware residents. The population of Delaware is growing.[91,92] Delaware's proportion of senior residents is also increasing.[93] The incidence of strokes in our state is likely to increase, with concomitant effects on emotional adjustment. Psychological sequelae of stroke such as PSD are treatable and perhaps in the not-too-distant future, also preventable. Despite the promising trends in assessment and therapies, the efforts to identify and treat emotionally afflicted patients following stroke are suboptimal across the nation.

Ideally, all patients with stroke should be screened for potential post-stroke depression as feasible. Screening at multiple time points over the course of a patient's recovery appears to be practical.[94] Following initial screening, re-assessment at multiple specified time points across the continuum of care (e.g., acute hospital care, rehabilitation transfer, discharge to subacute facility or home) and at follow-up physician and outpatient rehabilitation therapy visits is helpful in identifying and treating patients with psychological sequelae. The use of the PHQ-2 and PHQ-9 for this population appears to be supported in the literature. Clinician follow-up with a more detailed clinical interview for those with positive mood screens can be arranged by a stroke care team. In the State of Delaware, many of the hospitals and clinics have behavioral health professionals available who can assist with emotional adjustment or can link patients to providers in the community. Several of the hospitals also offer virtual or in-person support groups for stroke survivors and their caregivers. Ongoing research addressing post-stroke emotional sequelae is critical to optimizing the care that we clinicians provide to our patients who may be suffering from the psychological effects of strokes. It is anticipated that the findings from well-designed studies will help with prevention of these emotional disorders in addition to refining effective treatments. These developments are anticipated to benefit Delaware residents seeking care for the challenging effects of cerebrovascular disorders.

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