

Post-stroke Mood and Emotional Disturbances: Pharmacological Therapy Based on Mechanisms

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Post-stroke mood and emotional disturbances are frequent and diverse in their manifestations. Out of the many post-stroke disturbances, post-stroke depression, post-stroke anxiety, post-stroke emotional incontinence, post-stroke anger proneness, and post-stroke fatigue are frequent and important symptoms. These symptoms are distressing for both the patients and their caregivers, and negatively influence the patient's quality of life. Unfortunately, these emotional disturbances are not apparent and are therefore often unnoticed by busy clinicians. Their phenomenology, predicting factors, and pathophysiology have been under-studied, and are under-recognized. In addition, well-designed clinical trials regarding these symptoms are rare. Fortunately, these mood and emotional disturbances may be treated or prevented by various methods, including pharmacological therapy. To administer the appropriate therapy, we have to understand the phenomenology and the similarities and differences in the pathophysiological mechanisms associated with these emotional symptoms. This narrative review will describe some of the most common or relevant post-stroke mood and emotional disturbances. The phenomenology, factors or predictors, and relevant lesion locations will be described, and pharmacological treatment of these emotional disturbances will be discussed based on presumable pathophysiological mechanisms.

Keywords Stroke; Depression; Emotion; Serotonin; Treatment

Introduction

Mood and emotional disturbances are frequent symptoms in stroke survivors.¹ These symptoms are distressing for both the patients and their caregivers, and negatively influence patient quality of life.^{2,3} Important mood/emotional disturbances include post-stroke depression (PSD), post-stroke anxiety, post-stroke emotional incontinence (PSEI), post-stroke anger proneness (PSAP), and post-stroke fatigue (PSF). Underlying factors and predictors of these emotional disturbances partially overlap, but are still different. The relationships between these phenomena and lesion locations differ when considering the different emo-

tional symptoms. Thus, these diverse emotional disturbances are pathophysiologically interrelated, but are different phenomena.

Studies have shown that these emotional disturbances have negative impacts on patients' clinical outcomes. PSD, for example, negatively influences later functional outcomes after stroke,⁴⁻⁸ decreases quality of life,⁹ leads to less efficient use of rehabilitation services,⁸ and increases mortality.^{10,11} Patients with PSF are more often unemployed, change their jobs,^{12,13} and fail to return to previous jobs¹³⁻¹⁶ than those without PSF. Although the overall negative impacts of PSEI and PSAP are less marked than those of PSD, they still lead to distress and embarrassment, impair certain domains of patients' quality of life, and increase

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caregiver burden.¹⁷

Fortunately, these mood and emotional disturbances can be treated or prevented by various methods, including pharmacological therapy. In order to administer the proper therapy, we have to understand the similarities and differences between the phenomenologies and pathophysiological mechanisms associated with these symptoms. Regrettably, these important symptoms have been underdiagnosed, neglected, and under-studied.

This narrative review will describe some of the most common or relevant post-stroke mood and emotional disturbances. The phenomenology, underlying factors or predictors, and relevant lesion locations will be described. I will also discuss pharmacological treatments for these emotional disturbances based on presumable pathophysiological mechanisms.

Depression and depressive mood

Symptom characteristics and prevalence

The symptoms of post-stroke depression or depressive symptoms include depressed mood, anhedonia, loss of energy, decreased concentration, and psychic retardation. Although somatic symptoms, such as decreased appetite and insomnia are common, they may in part be attributed to the stroke itself, medications, or comorbid diseases. Guilty feelings and suicidal ideations are less common than observed in primary depression.¹⁸

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition has been used for the diagnosis of PSD. It defines depression as depressed mood or anhedonia (loss of interest or pleasure) for 2 weeks or longer, in addition to the presence of at least four of the following symptoms: substantial weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, worthlessness or inappropriate guilt, diminished concentration, and indecisiveness. However, it remains controversial whether these criteria, validated in physically intact persons, can be used in stroke patients, especially in the acute setting. Thus, other interviewer-administered or self-completed depression case-finding or screening instruments are also used in the study of PSD. These include the nine-item Patient Health Questionnaire, The Center of Epidemiological Studies-Depression Scale, Hospital Anxiety and Depression Scale, the Hamilton Depression Rating Scale, the Beck Depression Inventory, and the Montgomery-Asberg Depression Scale.¹⁹

The prevalence of PSD ranges from 5 to 67%.^{1,20-25} The wide variability is due to different study settings, time since stroke, and the different criteria/methods used to diagnose PSD.²⁶ A meta-analysis of 61 cohorts involving 25,488 patients published in 2014 indicated that 31% of patients developed depression at some time point up to 5 years following stroke.²⁷

Generally, the prevalence of major depression decreases over time. In one study, PSD was present in 50% of the patients in the acute phase, but only in 12% of the patients at a one-year follow-up.²⁸ Another study reported the prevalence of depression as 30% at 3 months post-stroke. Of these patients, 60% were no longer depressed one year later.²⁹ In the author's recent study involving 478 patients with acute stroke, approximately 57% had depression (Montgomery-Asberg Depression Scale > 8) at the time of the stroke. This percentage rapidly decreased over time.³⁰

Factors associated with PSD

Although various factors have been reported to be associated with PSD, the results have been inconsistent. A recent systematic review included 23 studies with 18,374 participants, and reported that demographic characteristics (age and sex) were not consistently associated with PSD.³¹ There was also no consistent association between hemisphere of stroke, lesion location, or pathological subtype, and depression. A history of depression before stroke was associated with PSD in four of seven studies, while cognitive impairment was associated with depression in two of four studies.

Based on the literature, the most consistent factors associated with PSD are severe stroke, and early or late physical disability. In our recent study, changes in Montgomery-Asberg Depression Scale scores were well-correlated with improvements in neurological impairment.³⁰ It seems that patients' acute depressive symptoms are related to physical dysfunction, while PSD at the chronic stage has an additional psychosocial component.^{21,32}

Lesion location

Robinson emphasized the role of left frontal lesions in producing PSD.²⁸ However, other studies have shown heterogeneous results,³³⁻³⁵ and one systematic review failed to find an association between lesion location and PSD.³⁶ We have shown that fronto-lenticulocapsular-brainstem base lesions are related to PSD.¹ An important confounding factor in these studies is the variability in time since stroke.³⁷ One study found that the association between left anterior cortical stroke and PSD was apparent at the acute stage, but not the subacute or chronic stages.³⁸ Higher lesion volumes, cerebral atrophy, silent infarcts, and white matter lesions may also be associated with a higher risk of PSD.^{32,39-41}

Pathophysiology

The close relationship between PSD and neurological deficits,¹ and between changes in Montgomery-Asberg Depression Scale scores and neurologic improvement,³⁰ suggests that PSD may be a psychological, reactive depressive symptom associated with sudden functional deficits. When there are prolonged functional

deficits, subsequent familial and social issues may perpetuate PSD.⁴² The presence of PSD may also be dependent on the patients' personality traits and environmental factors, such as social support, economic matters, job stability, etc.⁴²

However, there still are patients whose depression is not readily explained by neurological changes. For instance, patients with transient ischemic attacks or minor strokes can still have PSD.⁴³ The possible role of anterior frontal lobe damage and the involvement of the frontal-basal ganglia brainstem pathway in PSD development suggest alterations in neurotransmitter systems, such as serotonergic, adrenergic, and dopaminergic systems.¹ It is generally likely that patients with PSD have symptoms due to mixed mechanisms.

Treatment

In 2008, two Cochrane reviews were published regarding the prevention⁴⁴ and treatment⁴⁵ of PSD. The authors identified 14 prevention trials involving 1,515 people, and reported a small effect for psychological intervention. However, there was no evidence of an effect due to antidepressant drugs. Nevertheless, a few trials of antidepressant drugs^{46,47} published afterwards have shown some benefit of antidepressant drug use. The Cochrane review of treatment trials identified 16 trials involving 1,655 subjects. Although antidepressant drugs (13 trials) produced improvements in depressive symptoms, it is uncertain whether they lead to higher rates of remission for depression. The use of antidepressants increases gastrointestinal and central nervous system side effects. There was no evidence for effectiveness of psychological therapies alone for the treatment of PSD.

Therefore, although antidepressants seem to be effective for the treatment of PSD, the evidence is not robust. Nevertheless, European⁴⁸ and American⁴⁹ guidelines recommend pharmaceutical treatment, such as selective serotonin-reuptake inhibitors (SSRI) or tricyclic antidepressant drugs for patients with PSD, along with monitoring for effectiveness and side effects. It is recommended that treatment be continued for at least 6 months after initial recovery.

Post-stroke anxiety

Prevalence and characteristics

Post-stroke anxiety disorders have received relatively little attention compared to PSD. The core symptoms of post-stroke anxiety are excessive anxiousness or worry, and difficulty in controlling worries. Criteria from The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition require three or more of the following in addition to the above symptoms: restlessness, decreased energy, poor concentration, irritation, nervous tension,

and insomnia. Beck Anxiety Inventory, Hamilton Anxiety and Depression Scale, Hospital Anxiety and Depression Scale, and the General Health Questionnaire-30 have also been used for the study of post-stroke anxiety.^{50,51}

The prevalence of post-stroke anxiety, with or without PSD, is higher in hospital settings (acute stroke patients: 28, 15–17, and 3–13%, respectively; stroke survivors: 24, 6–17, and 3–11%, respectively) than in community studies (11, 8, and 1–2%, respectively).²⁶ While one study showed that the prevalence of post-stroke anxiety decreased over time (33% at 3 months, 18% at 2 years),²² another study reported no such changes over 3 years after stroke.⁵² Post-stroke anxiety tends to last longer when it is associated with PSD.⁵² A recent systematic review⁵³ involving 39 cohorts and 4,706 patients showed that 24% of patients with stroke had anxiety symptoms and 18% had an anxiety disorder in the first 5 years after stroke.

Because early-onset anxiety is more often associated with previous psychiatric disorders than late-onset anxiety, it has been proposed that early-onset anxiety may be a recurrence/exacerbation of a pre-stroke generalized anxiety disorder.⁵¹

Although post-stroke anxiety by itself does not influence functional or cognitive recovery, it is associated with worse social functioning and quality of life. In a systematic review,⁵³ the quality of life was negatively correlated with anxiety in four of five cohorts. Patients with post-stroke anxiety and PSD were worse in activities of daily living at 1- and 2-year follow-ups than patients with post-stroke anxiety alone.⁵⁴

Factors associated with post-stroke anxiety

Post-stroke anxiety is closely associated with PSD.⁵³ Early studies proposed that following left hemispheric strokes, post-stroke anxiety with PSD is associated with cortical infarcts. On the other hand, following right hemispheric strokes, post-stroke anxiety without PSD is associated with posterior infarcts.⁵⁵ However, a recent meta-analysis showed that there is no association between post-stroke anxiety and lesion location.⁵³ Furthermore, no associations were observed with age and sex. Thus, the factors associated with anxiety in patients with stroke without PSD remain unknown.

Treatment

Antidepressant/antianxiety drugs alone or with psycho-behavioral therapy may reduce anxiety symptoms. However, because there are no randomized, placebo-controlled trials, there is not enough evidence regarding the management of post-stroke anxiety.⁵⁶

Emotional incontinence

Prevalence and characteristics

Since Wilson described patients with uncontrollable outbursts of involuntary laughing or crying as having "pathologic laughing and crying",⁵⁷ these abnormal emotional displays have been described using a variety of terminologies: pseudobulbar affect, emotionalism, lability of mood, emotional incontinence, and involuntary emotional expression disorder.⁵⁸

Typically, patients show excessive and inappropriate crying or laughing without apparent motivating stimuli, or in response to stimuli that would not normally evoke such responses. The episodes are sudden, episodic, and uncontrollable. Although early reports emphasized the importance of these incongruent or contradictory emotional stimuli, and the "unheralded", "uncontrollable" nature of symptoms,⁵⁹ recent studies have found that symptoms are more often triggered by appropriate and congruent stimuli.^{1,60} Although some authors have distinguished strict pathological laughing and crying from milder emotional lability,⁵⁹ more recent studies^{61,62} have reported that these two conditions differ in a quantitative rather than a qualitative way. With this consideration, we will use the broad term post-stroke emotional incontinence (PSEI) in this article.

The most frequently used diagnostic criteria are those of House,⁶⁰ followed by those from Kim.¹ In the acute/subacute stage of stroke, PSEI prevalence has been reported to vary from 6% to 34%.^{1,60,63-70} The heterogeneous results are due to different diagnostic criteria, the timing of assessment, and characteristics of study populations. There have been few studies that examined the longitudinal course of PSEI. One report indicates that the prevalence of PSEI is 15% one month post-stroke, 21% at six months post-stroke, and 11% at twelve months post-stroke.⁶⁰

Factors and lesion locations associated with PSEI

Severe motor¹ and neurologic dysfunction,^{67,69} lesion location,^{1,63,70} and the presence of depression^{1,60,65} are reported to be related to PSEI. We reported that lesion location (subcortical area) is the only factor associated with PSEI at the time of admission, whereas functional status, serotonin polymorphisms, and low social support were related to PSEI at three months post-stroke.⁷⁰

Studies using computed tomography and magnetic resonance imaging have shown that lenticulocapsular^{71,72} and brainstem lesions⁷² are closely related to PSEI. We studied 148 patients with unilateral strokes who were identified using computed tomography and magnetic resonance imaging and found that the anterior cortex-internal capsule/basal ganglia-ventral brainstem circuitry is closely related to PSEI.¹ Patients with lesions in the thal-

amus or cerebellum also occasionally exhibited PSEI. Although this lesion location is similar to that producing PSD, PSEI seems to be more closely related to subcortical (basal ganglia and pontine) lesions.¹

Pathogenesis

Wilson proposed that pathological crying and laughing is caused by the release (or disinhibition) of a brainstem fasciorespiratory control center for emotional expression secondary to lesions of descending regulatory pathways.⁵⁷ Previous studies have described patients presenting with PSEI due to lesions of the ponto-cerebellar pathway, and hypothesized that the cerebellum may play a modulatory role and adjust the execution of laughing or crying to cognitive and situational contexts.⁷³⁻⁷⁸ Rabins and Archinegas⁷⁹ suggested that a complex cortico-limbic subcortical-thalamic-ponto-cerebellar system contributes to the expression of emotions, and any deficit in this system may lead to PSEI.

Neuroanatomical lesion studies suggest the involvement of serotonergic fibers,^{66,80,81} that ascends from the brainstem raphe nuclei to limbic forebrain structures and then project through the basal ganglia to the frontal cortex. Furthermore, serotonin transporter binding ratios in the midbrain and pons regions are lower in patients with stroke with PSEI than in those without PSEI.⁸² Finally, serotonin gene polymorphisms were found to be related to the development of PSEI.^{69,70}

Other neurotransmitters that may also be involved include dopamine and glutamine, which may have roles in regulating the influence of the motor cortex on the brainstem laughing/crying centers.^{79,83-85} The balance between glutamatergic excitation and inhibition is in turn modulated by other neurotransmitter systems, such as dopamine, serotonin, acetylcholine, and sigma receptor systems.⁷⁹ Non-competitive glutamate receptor antagonists, such as dextromethorphan stabilize glutamatergic neurotransmission,⁸⁶ and have been found to be effective in the treatment of pathological laughing and crying in amyotrophic lateral sclerosis⁸⁵ and multiple sclerosis,⁸⁷ perhaps due to their effect on sigma-1 receptors. As activation of sigma-1 receptor agonists increases the serotonergic function of the dorsal raphe nucleus,⁸⁸ dextromethorphan may also modulate the serotonergic system.

Treatment

A recent Cochran review confirmed that SSRIs are effective in reducing the frequency and severity of PSEI.⁸⁹ In five randomized controlled trials,⁹⁰⁻⁹⁴ SSRI administration was effective in alleviating PSEI. In addition, two randomized controlled trials have shown that tricyclic antidepressants are effective in treating PSEI.^{95,96} In the author's view, SSRIs should be the first option for PSEI treatment, because they are better tolerated in stroke pa-

tients and more promptly reduce PSEI symptoms than tricyclic antidepressants.

There have been small studies that have used the selective adrenergic receptor inhibitors reboxetine,⁹⁷ venlafaxine,⁹⁸ mirtazapine,⁹⁹ and lamotrigine.¹⁰⁰ The mechanisms of action of these agents may involve the direct or indirect augmentation of serotonergic function. As discussed earlier, levodopa and amantadine may be effective in treating PSEI. Due to limited data, these selective adrenergic receptor inhibitors and dopaminergic drugs are currently reserved for patients who fail to respond to SSRIs.⁹⁹ Dextromethorphan/quinidine (Nuedexta[®], Avanir) is another potentially useful drug for the treatment of PSEI.^{85,87} Dextromethorphan is a sigma-1 receptor agonist, and adding quinidine sulfate increases the bioavailability of dextromethorphan.

Post-stroke aggression and anger proneness

Symptom characteristics and prevalence

Stroke patients may show aggressive behaviors including hitting or hurting others, kicking, biting, grabbing, pushing, throwing objects, etc. Their verbal behavior also includes cursing, screaming, making noises, hostile muttering, etc. This overt aggression is observed usually during the acute stage in patients. However, simple anger-proneness or inability to control anger and aggression is a much more commonly observed symptom. Patients become more irritable, impulsive, hostile, and less tolerable. They easily anger at their spouses and other family members regarding trivial matters.¹⁰¹ Therefore, these symptoms may be described as post-stroke anger proneness (PSAP).⁹⁴

The PSAP has been studied using various tools, such as the Spielberger Trait Anger Scale, Present State Examination, NEO Personality Inventory Revised, and the Emotional Behavior Index.¹⁰¹⁻¹⁰⁴ PSAP is found to be present in 15-35% of patients during the acute stage,^{102,103,105,106} and in 32% of patients in the subacute stage.¹⁰¹ Although these results are not comparable due to different study settings and the different diagnostic tools used, we can at least conclude that anger proneness or aggressiveness is fairly common during both the acute and the subacute stages of stroke.

Associated factors, lesion locations, and pathophysiology

Studies have shown that motor dysfunction, dysarthria, high National Institute of Health Stroke Scale scores, previous stroke, premorbid neuroticism personality trait, history of depression, and low monoamine oxidase A activity are related to PSAP.^{101,103,104,106} Kim et al.¹⁰¹ emphasized that PSAP is more closely associated with

PSEI than PSD and that the distribution of lesion locations associated with PSAP is similar to that of lesions associated with PSEI (fronto-lenticulocapsular-pontine base area).

Therefore, similar to PSEI, serotonergic dysfunction seems to play a role in the development of PSAP. Because PSAP is also associated with severe neurologic dysfunction, depression, and a previous history of stroke, some of the patients' anger may be a manifestation of depression or frustration. Thus, PSAP may be a multi-factorial phenomenon related to reactive behavioral changes associated with functional deficits and repeated strokes, serotonergic dysfunction due to brain damage, or genetic polymorphisms involving monoamine oxidase A.¹⁰¹

Treatment

SSRIs such as fluoxetine¹⁰⁷ and citalopram¹⁰⁸ are of benefit in the treatment of aggressive behavior in patients with personality disorder or dementia. Beta adrenergic antagonists¹⁰⁹ and lithium¹¹⁰ may reduce aggressiveness in patients with brain injury. However, clinical trials in patients with stroke are very rare. In our double-blinded study, anger scores were significantly reduced after fluoxetine therapy in patients with subacute stroke.⁹⁴ In the author's more recent study involving 478 patients, escitalopram was effective in the prevention of anger-proneness when administered during the acute stage.³⁰

Post-stroke fatigue

Symptom characteristics and prevalence

Staub and Bogousslavsky¹¹¹ defined fatigue in stroke patients as 'a feeling of early exhaustion developing during mental activity, with weariness, lack of energy, and aversion to effort'. Fatigue can be further distinguished by its onset: fatigue during the acute stage vs. chronic, persistent fatigue. It can also be classified based on different constructs: exertion vs. mental fatigue.¹¹²

Although there is no fatigue scale that fully considers the complex nature of PSF, several instruments have been developed to measure PSF: the Fatigue Assessment Scale,¹¹³ the Fatigue Impact Scale,¹¹⁴ the Checklist of Individual Strength,¹¹⁵ the Visual Analogue Scale,^{116,117} the Chalder fatigue scale,¹¹⁸ the Multidimensional Fatigue Symptom Inventory,¹¹⁹ and the Fatigue Severity Scale.^{12,116,117,120-122}

The prevalence of PSF ranges from 23% to 75%.¹¹² This wide range is attributable to differences in the definition of PSF, the time elapsed since stroke, and the characteristics of patients. In a systematic review of nine longitudinal cohort studies, the authors reported that the prevalence of fatigue decreased with time after stroke in seven studies, but increased in two studies.¹²³

Factors associated with post-stroke fatigue

Neurologic deficit is one of the most important factors related to PSF.^{12,13,119,124,125} However, the association may at least in part be attributed to associated depression. Studies have shown that the significant association between disability and PSF in the subacute state is lost after controlling for the effects of depression during the chronic stage.^{14,126} Medical co-morbidities such as hypertension,¹²⁷ medications such as sedative drugs¹²⁸ or antidepressants,^{129,130} decreased appetite,¹² and sleep disturbances,^{122,125,131-136} may result in PSF. In addition, post-stroke pain,^{133,137,138} and pre-stroke fatigue have been found to be associated with PSF.^{12,122,124,128,130,139}

Although patients with PSF are often depressed,^{12,111,114,121,122,132,140} many PSF patients do not have depression.^{12,13,111,114,115,118,124} Although one study reported an association between PSF and suicidality,¹⁴¹ PSF patients rarely express worthlessness and hopelessness. The impact of depression on PSF may differ according to the stage of stroke. While neurologic disability leads to exertional fatigue during the early stage of stroke,¹⁴ depression seems to play a more important role in chronic and mental fatigue.^{142,143} Thus, depression may be a factor in prolonged fatigue.¹³⁴ Impairments in some domains of cognition, such as attention deficits,¹⁴ slow mental processing,^{15,144,145} and memory dysfunction,¹⁵ seems to be associated with mental fatigue.

Studies have shown that PSF is related to damage to the medial prefrontal cortex,¹⁴⁶ basal ganglia,¹²¹ and the brainstem/thalamic reticular formation.^{111,147,148} This suggests that alterations in neurotransmitters such as dopamine or adrenaline may lead to PSF.^{147,148} However, more recent MRI-based studies have found no association between PSF and lesion location.^{12,114,115,119,143,149} Chronic inflammation and altered immune responses after stroke may also be involved in PSF.¹⁵⁰

Treatment

A double-blinded placebo-controlled trial involving 83 patients with PSF showed that fluoxetine was not effective in improving PSF.¹¹⁶ Another study showed that duloxetine, citalopram, and sertraline did not relieve PSF.¹⁵¹ Thus, SSRIs may not be effective for PSF. Modafinil, a drug originally used for patients with hypersomnia or narcolepsy, was used in a recent randomized, placebo-controlled trial.¹⁵² Forty-one patients were treated with either 400 mg modafinil or placebo. There was no difference in the primary outcomes or Multidimensional Fatigue Inventory-20 general fatigue scores 90 days post-stroke. However, modafinil improved PSF, as measured by the Fatigue Severity Score, a secondary outcome ($P=0.02$). Thus, more studies are needed to confirm the efficacy of modafinil as a treatment for PSF. The neurobiochemical effects of modafinil remain unclear. It

may affect dopamine and norepinephrine transporters. It is also known to have some effects on the serotonin, glutamate, orexin, and histamine systems.¹⁵³

Summary

Post-stroke mood and emotional disturbances are common and manifest in diverse manners. The phenomenology, predicting factors, pathophysiology, and response to pharmacological treatments are different, although there are also factors that are in common. PSD appears to be associated with complex pathophysiological mechanisms involving both psychological/psychiatric problems associated with patients' functional deficits and neurochemical changes secondary to brain damage. Therefore, although antidepressants, and especially SSRIs, are considered to be the management options of choice, their benefits are not robust. It remains uncertain whether pharmacological treatment in stroke patients is needed to prevent PSD or perhaps to improve neurological outcomes.

PSEI is more closely associated with lesion location and consequent alterations in neurotransmitters, notably serotonin. Thus, PSEI tends to respond more to SSRIs compared to PSD. Although PSAP is also a complex phenomenon, it seems to have better responsiveness to SSRIs than PSD. PSF is a common and disabling symptom. Although PSF is closely associated with PSD, it is also causally related to multiple factors, including functional impairment, co-morbid diseases, and perhaps, multiple neurotransmitter changes. Thus, the benefits of pharmacological therapy are unproven, and treatment may have to be individualized according to the causative factors present in each patient. Adrenergic/dopaminergic drugs such as modafinil may be used in some patients.

Recognizing these emotional disturbances is important because they are often treatable. Proper management may improve patients' quality of life in a prolonged manner, even after the cessation of treatment.¹⁵⁴ Undoubtedly, more research is needed to improve the management of post-stroke mood and emotional disturbances.

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