Neuropsychiatric Complications of Cerebrovascular Disease

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Abstract This rendition delves into several of the neuropsychiatric manifestations of cerebrovascular events, including mania, anxiety, apathy, disturbance of the sleep–wake cycle, fatigue, sexual dysfunction, cognitive impairment, empathic impairment, theory of mind, social-emotional dysfunction, involuntary emotional expression disorder, irritability, psychosis, agitation, and depression. The focus is on the manifestations of these presentations for proper diagnosis, as well as the lesion localization particular to the respective symptomatology. Furthermore, the hope is that this contribution allows for a greater awareness regarding the complications of stroke and brings attention to the sequelae from which its victims suffer.

Keywords Cerebrovascular disease • Involuntary emotional expression disorder • Neuropsychiatric complications • Stroke • Theory of mind

Introduction

Stroke is the third leading cause of death in the United States, the second leading cause of death worldwide, and a major cause of long-term physical and mental disability in stroke survivors. With estimates by the American Stroke Association of 750,000 strokes occurring annually in the United States, there are likely about 4.5 million stroke survivors in America today [1]. Additionally, economic costs of

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stroke in the United States have been estimated to be at least $43 billion each year [2]. A major portion of these costs are allocated toward the treatment of secondary complications, especially disability caused by depression, cognitive impairment, and other neuropsychiatric complications.

The symptomatology of stroke survivors is an array of comorbid symptoms, many of which were previously assumed to be of the same etiology or interrelated. However, given recent research among this patient population, more understanding has been gathered regarding the individual pathogenesis for many of these complications. Some of the neuropsychiatric sequelae secondary to cerebrovascular disease and their hypothesized mechanisms will be discussed here as the individual entities that they are. It is in this way that the clinician can more closely examine each symptom the individual patient suffers from and appropriately treat the exact cause of that symptom rather than approaching collective complaints and applying a generalized treatment plan. This approach may prove to be useful in the rehabilitation and treatment of neuropsychiatric complications in stroke patients leading to historical recovery in the quality of life of these patients and their loved ones.

Mania

Mania secondary to stroke, given its rarity and likely underdiagnosis, has limited appearance throughout the neuropsychiatric literature. In prior studies looking at neuropsychiatric complications following stroke, enrolled patients uncommonly suffered from poststroke mania in comparison to other psychiatric complaints [1]. Of two major studies investigating poststroke complications, one following 700 consecutive stroke patients [3] and another looking at 661 stroke survivors [4], only 6 patients in total between the two studies presented with mania secondary to stroke. Additionally, in two other considerably large community studies, the Oxfordshire Community Stroke Project and the Perth Community Stroke Project, both of which were investigating the prevalence of neuropsychiatric disorders following stroke, zero patients were found to suffer from poststroke mania [1]. When witnessed, however, mania secondary to stroke demonstrates very similar symptomatology in comparison to patients suffering from primary mania. These frequently include elation, pressured speech, insomnia, grandiosity, and flight of ideas with racing thoughts. Although the prognostic characteristics of poststroke mania are limited, it does appear that a family history of mood disorder is correlated with a higher risk of mania after stroke [1].

Despite the infrequency of poststroke mania, the lesion localization in patients suffering from secondary mania is more definitively understood. Most hypotheses related to mania and stroke location concur that right hemispheric strokes are likely responsible for the manifestation of this symptom. Prior studies have discussed that lesions in the right hemisphere lead to anterior limbic circuit dysfunction involving the orbitofrontal and basotemporal cortex in addition to the head of the caudate and dorsomedial thalamic nucleus. It has been hypothesized that a more generalized cerebral distribution may be responsible for the rarity of this symptom, given that both subcortical and limbic involvement is necessary for manic symptoms [1].

The neuropathology of poststroke manic symptoms appears to be due to a contralateral release phenomenon. It is likely that after a right hemispheric lesion there is subsequent activation of the contralateral left hemisphere. Both Starkstein and Robinson, as well as Mimura et al., have discussed the concept of left hemisphere release in postlesion mania [5]. This hypothesized pathogenesis originated during a case involving a patient who suffered from acute onset of poststroke mania after a right hemispheric infarction in the middle cerebral artery distribution. This patient's prestroke medical records included a single-photon emission computed tomography (SPECT) study, which provided a postinfarction comparison. In evaluation of these SPECT studies, it became evident that there was a definite pattern of left-sided orbitofrontal hyperperfusion associated with severe right frontal hypoperfusion only observed during the patient's poststroke manic episodes [5].

Given the rarity of this complication, information regarding its treatment is limited. Lithium has been the most commonly used therapy for patients suffering from mania secondary to stroke. However, pharmaceutical studies focused on poststroke mania are scarce to none, leaving only published case reports as the single source of reference relating to its therapy. Treatment modalities discussed throughout the literature include the use of olanzapine, carbamazepine, and valproic acid, the last of which has demonstrated the greatest documented therapeutic results. Filardi da Rocha et al. reported the use of 750 mg/day of valproic acid with good improvement of symptomatology in their 57-year-old male patient with mania secondary to a severe right temporal-parietal lobe stroke [6]. Because of the infrequency of reports investigating poststroke mania, clinicians must continue to thoroughly evaluate their stroke patients in order to ensure that this diagnosis is not missed. Once the diagnosis of mania is made, much benefit could be gained for future stroke survivors if effective treatment options are compared and documented by the neuropsychiatrists treating these patients.

Anxiety

The DSM-IV-TR criteria for primary generalized anxiety disorder includes the presence of a sustained worrying state, in addition to a minimum of three other anxiety symptoms, such as concentration difficulties, irritability, muscle tension, sleep disturbances, restlessness, and decreased energy, for a period of at least 6 months.

Although not as prevalent as poststroke depression (PSD), anxiety has also come to be regarded as a major neuropsychiatric complication severely impacting the daily functioning and quality of life of stroke survivors. In 1997, Robinson reported a mean prevalence of poststroke anxiety to be 14.4%, with some studies reporting up to 28%; however, with improved screening and diagnosis, this value is surely more common today [7]. Recent studies have demonstrated that patients who present with anxiety disorder after suffering a stroke are more likely to have impairment in psychosocial functioning and activities of daily living (AODL) than patients with generalized anxiety disorder not suffering from cerebrovascular disease [7]. Additionally, these patients were at a greater risk of comorbid insomnia and depression than their nonstroke

counterparts. These findings are not only significant for the increased burden of disease on the patient but have ramifications regarding the prescribing of sleep-promoting and anxiolytic drugs, which also contribute to further difficulty in daily functioning.

In contrast to studies investigating PSD, a previous history of migraines and/or epilepsy before the insighting cerebrovascular event seem to increase the risk of poststroke anxiety [7]. In addition, anxiety secondary to stroke was related to the following demographic and clinical factors: smoking, migraine, epilepsy, previous mental disorders, comorbid depression and insomnia, stroke severity, and impairment in psychosocial functioning and in AODL. Women also seem to be more likely to suffer anxiety secondary to stroke than men, although reasons for this finding are still under investigation.

Patients diagnosed with generalized anxiety disorder secondary to stroke demonstrated lesion localization predominantly in the territory supplied by anterior circulation. Stroke survivors who suffered a lesion in the anterior circulation demonstrated worse scores on the anxiety scale than those survivors with lesions in the posterior circulation [8]. This finding may support recent hypotheses that suggest a distinction between the mechanism of poststroke anxiety and generalized anxiety. Several recent studies report that although left hemispheric strokes were found to cause comorbid depression and anxiety disorders, isolated anxiety secondary to stroke was localized to right hemispheric lesions [5], although a more specific lesion localization has yet to be identified.

Treatment modalities used for patients suffering from poststroke anxiety have primarily been based on those implicated for patients with primary generalized anxiety disorder. Studies on therapy for anxiety secondary to stroke are limited. Thus far, the recommended treatment is benzodiazepines, excluding the elderly population given reports of significant side effects. The preferable therapeutic modality in elderly patients who are unable to tolerate benzodiazepines are buspirone and selective serotonin uptake inhibitors (SSRIs).

Apathy

Apathy can be defined as lack of emotion, feeling, or concern, not attributable to an alteration in consciousness or cognition. It is prevalent in both the general psychiatric patient population, as well as in stroke survivors, with implications in the functional recovery and rehabilitation of these patients. In patients who have suffered from first-ever and/or recurrent strokes, there exists a frequency of apathy of approximately 23% [9]. This effect can be evaluated through the interpretation of the Apathy Scale proposed by Starkstein et al., which is a modified version of the apathy evaluation scale originally designed by Marin et al. Interestingly, the occurrence of depression is not significantly different when comparing patients with and without apathy, as one might expect. Poststroke apathy has been demonstrated more commonly in older patients when compared to nonapathetic stroke survivors, as well as in those who suffered from an ischemic, rather than a hemorrhagic, stroke [10].

Symptomatic lesions have been found in even distribution bilaterally throughout the brain among apathetic and nonapathetic stroke patients. Continued research is warranted by the recurrent inconsistencies regarding lesion localization in patients suffering from poststroke apathy. Chemerinski et al. reported a collective literature review demonstrating the occurrence of 93 left-sided lesions, 77 right-sided lesions, and 94 bilateral strokes resulting in secondary apathy [1]. Several factors that have been previously correlated with apathy following stroke include cognitive dysfunction, advanced age, deficits in AODL, decreased attention and information processing, and poor fluency [1]. When examining the functional level of stroke survivors, apathetic patients demonstrate a significantly lower recovery level in aspects of self-care. This aspect is of great importance when evaluating caregiver burden and the long-term ramifications that these patients and their families face during stroke rehabilitation.

Treatment recommendations for poststroke apathy include the use of various stimulating antidepressants, such as fluoxetine, for first-line therapy. Additionally, other stimulating agents, such as amphetamine, methylphenidate, selegiline, and bupropion have been used successfully to treat apathy; however, only in case reports. Recent studies have examined the role of cholinesterase inhibitors in the treatment of apathy given the activating properties of these agents and the correlation with poststroke apathy and cholinergic deficits [11].

Disturbance of the Sleep–Wake Cycle

Sleep disorders have recently become an area of medical interest given their significant impact on a patient's daily living. Pathology of sleep is a spectrum of abnormalities that affect sleep time, the sleep cycle, and breathing and activity during sleep. One example includes dyssomnias, such as insomnia and hypersomnia, in which a patient has an alteration in the amount of time asleep within a given 24-h period. On average, 7–9 h of sleep per night is considered adequate by the National Sleep Foundation in the United States, although there are some normal variants that slightly deviate from this amount. Chen et al. defined short-sleep duration as a night's sleep of 6 h or less and a long-sleep duration as more than 9 h of sleep [12]. Other sleep disorders involve disruption in the normal pattern of the sleep cycle between non-REM and REM (rapid eye movement sleep). Abnormalities within either the amount or cycling of the sleep cycle can consequentially lead to deficits in attention, memory, daily functioning, an increase in accidents, and a diminishment of overall health.

In patients who have suffered stroke, the reduction in quality of life has evoked great focus. Although the etiology of this change is multifactorial, disturbance of the sleep–wake cycle in these patients appears to be a significant contributor. Long-term follow-up of stroke survivors who have suffered from both ischemic stroke and/or subarachnoid hemorrhage reveals difficulty in initiation of sleep, irritability, loss of interests, poor concentration, fatigue, and falling asleep at inappropriate times throughout the day. Assessment of functional outcome, and therefore quality of life,

has been evaluated in stroke patients using the Rankin Scale, a 6-point handicap scale focusing on restrictions of lifestyle in coordination with polysomnographic studies.

It appears that up to one-third of stroke survivors suffer from either insomnia, excessive daytime sleepiness, or both, resulting in lower values when scoring quality of life. It is important to note that sleep disturbances caused by stroke must be differentiated from sleep disturbances that are secondary to other neuropsychiatric complications of stroke, such as depression. For example, Schuiling et al. reported that sleep disturbances resulting from depression are characteristically demonstrated by short-REM sleep latency and an increased amount of REM sleep overall, whereas sleep disturbances that do not show this pattern, but occur after stroke, are more likely a result of the stroke alone and may secondarily lead to the initiation of sleep disturbance depression [13]. Landau et al. demonstrated lesion localization in patients with sleep disturbances secondary to stroke concentrated in the right pons, followed by bilateral pontine strokes, and then left pontine lesions [14]. In patients diagnosed with restless leg syndrome following stroke, Kim et al. demonstrated lesion topography predominantly in subcortical regions, such as the pyramidal tract and basal ganglia–brainstem axis [15]. This result reinforces that compromise of cerebral perfusion in areas of the brain controlling motor function and the sleep–wake cycles may result in restlessness symptoms. Treatment modalities available for these symptoms include dopamine agonists, which have delivered relatively significant relief in symptoms [15].

Fatigue

Fatigue has been known to be a common sequelae in stroke survivors, with a prevalence ranging from 38% to 68% [16]. Treating this phenomenon has proven to be quite challenging given the lack of established standards in its measurement and difficulty in determining its exact etiology. Additionally, the diagnostician must take into consideration other possible contributing factors associated with fatigue from which numerous stroke patients suffer from months to years after the inciting event; these include mental factors, such as depression and anxiety, but also might be related to physical deconditioning and gross motor deficits. Because the etiology of fatigue has proven to be so complex, it is not until recently that research has began to control for some of these confounding factors and evaluate a more central origin of fatigue in stroke survivors.

In a study investigating fatigue in stroke survivors, patients who suffered from minor strokes were compared to those who experienced a transient ischemic attack (TIA). While previous studies suggested that fatigue after stroke was attributable to compensatory behaviors related to gross neurological deficits, the comparison used in this study demonstrated that poststroke fatigue may be of central origin rather than physical sequelae secondary to increased effort required after suffering a stroke [16]. By investigating patients who suffered from minor rather than major strokes, there were minimal to no residual neurological deficits to which secondary poststroke fatigue might be attributable. These results were the first set of published data investigating fatigue in relationship to stroke using this approach.

The study evaluated 149 patients: 73 status post minor stroke and 67 status post TIA. Demographic characteristics, recent life events, vascular risk factors, medications, and mental and physical disabilities were all variables that were controlled among the two patient groups. Fatigue was evaluated at 6 months after minor stroke or TIA using the Chalder Fatigue Scale [17]. The results of the study demonstrated that patients who suffered from a minor stroke had a 56% fatigue prevalence in comparison to the TIA patients with a prevalence of 29%. This finding is one that should serve to motivate neuropsychiatrists and other clinicians to move toward the consideration of a central mechanism underlying fatigue in patients who have suffered a stroke. Additionally, collaborative efforts between researchers, physicians, and pharmaceutical experts should investigate central-acting treatment modalities for these patients. Treatment is mainly symptomatic, with the use of stimulating agents, in addition to treating concurrent neuropsychiatric complaints.

Sexual Dysfunction

In adult patients, cerebrovascular disease causes greater secondary impairment than any other major illness in the United States. Perhaps one of the most limited areas of investigation among poststroke complications is that of sexual dysfunction. Historically, the pathogenesis of sexual dysfunction was viewed as predominantly a psychogenic disorder; however, after more closely investigating patients suffering from various sexual impairments, additional hypotheses have begun to reveal themselves. Prior studies have demonstrated that sexual dysfunction after stroke is multifactorial, with both organic and psychological etiologies at its origin. Organic influences on sexual function include certain comorbid medical conditions, such as diabetes, hypertension, and cardiac disease. Psychosocial factors include loss of self-esteem, fear of another stroke, and changes within the spousal relationship [18]. More recently, physicians have recognized that in stroke patients there likely exists both a psychogenic and neurogenic pathophysiology to erectile dysfunction.

Although most research on sexual dysfunction has involved male patients, there is no doubt that this is a complication experienced by both male and female patients. One Scandinavian study reported a decline in sexual desire in three-quarters of male stroke patients and two-thirds of female stroke patients [19]. From previous studies, it is evident that major complications of concern include decreased sexual desire in both male and female patients, diminished vaginal lubrication and orgasm in female patients, and impairment in erection and ejaculation in men [18]. Additionally, these poststroke consequences extend beyond the individual to also affect their intimate relationships with their partners.

A recent study investigating sexual dysfunction in male stroke patients was aimed at correlating this impairment with brain localization of the stroke lesions [20]; this appears to be the first study to correlate specific aspects of sexual dysfunction with localization of strokes. The comparison was made between 109 male stroke patients and 109 aged-matched controls. A five-item version of the International Index of Erectile Function was use to evaluate changes in sexual desire, ejaculatory function,

and sexual satisfaction after stroke. These results were then analyzed with the location of the respective patients' brain lesions.

Overall, the study demonstrated a significant decrease in erectile function in the stroke patient group. Frequency of sexual intercourse and sexual desire were both significantly reduced in this patient group. The diminished frequency in intercourse was found to be most commonly (almost 60%) secondary to the lack of sexual desire after stroke. More specifically, stroke patients suffering from ejaculation disorders demonstrated lesions in the right cerebellum. Additionally, patients experiencing decreases in sexual desire showed imaging correlations such that their brain lesions were concentrated to the left basal ganglia. Overall, these findings were able to localize patterns with certain aspects of sexual dysfunction. A larger and more inclusive study would likely be helpful in confirming these associations between sexual dysfunction and the respective neuroanatomy.

The common implication among studies evaluating poststroke sexual dysfunction is such that these impairments should be more frequently addressed and aggressively treated during the rehabilitation process in stroke survivors so that they can enjoy a healthier quality of life and continue to share and participate in intimate relationships with their partners. Although poststroke rehabilitation has shown to help in the recovery of sexual functioning, additional therapies used for sexual dysfunction unrelated to stroke may also be used.

Cognitive Performance

Neuroscience has demonstrated the association between increased cognitive impairment following infarction; however, the pathophysiology by which infarcts result in this cognitive dysfunction is incompletely understood. A popular hypothesis involves the disruption of the cerebral circuitry with resultant deficits in cognition, usually with the frontal-subcortical circuits being affected. Injury to these circuits results in deficits in memory, information processing, and executive dysfunction. Additionally, disruption of cerebro-cerebellar circuits often causes problems in higher cognitive functions.

In particular, many studies have examined the impact of location and number of infarcts on cognitive impairment. In a recent study by Saczynski and colleagues, three separate cognitive domains were investigated following the diagnosis of cerebral infarct: processing speed, memory, and executive dysfunction. In the 4,030 nondemented participants enrolled in the Age Gene/Environment Susceptibility – Reykjavik Study, it was found that those patients who suffered infarcts in multiple locations had slower processing speed, poorer performance in memory, and executive dysfunction in comparison to patients with infarcts concentrated to a single location. Interestingly, those participants who did suffer multiple infarcts within one region did not demonstrate any cognitive discrepancies from the noninfarct control group after model adjustment [21]. These findings are all independent of white matter lesions, brain atrophy, cardiovascular comorbidities, and depressive symptoms. Treatment modalities for post-stroke cognitive impairment include the use of acetylcholinesterase inhibitors, in addition to recent developments, such as the use of

repetitive transcranial magnetic stimulation (TMS). A focal lesion such as a stroke may produce a state of hemispheric imbalance. TMS can be used to repair this disequilibrium between the ipsi-lesional and contra-lesional cerebrum.

Involuntary Emotional Expression Disorder

The expression of human emotion allows individuals the potential to communicate feelings to those around them; however, the pathology of emotional expression can be consequentially devastating to an individual's relationship with loved ones, the overall functional quality of life, and the ability to relate, cope, and form new bonds. Although this emotional disinhibition syndrome is observed in association with numerous neurological conditions, its application to poststroke patients has become a growing area of interest and research. Given the importance of identifying and properly treating this neuropsychiatric condition, Cummings and colleagues proposed terminology and diagnostic criteria to be applied to this involuntary emotional expression disorder (IEED) [22]. IEED is defined as uncontrollable bouts of emotional expression that are incongruent with or disproportionate to how the patient actually feels at the time of the episode.

The current definition of IEED likely results from a single pathological mechanism but is inclusive of the following clinical observations: pathological crying and laughing, emotional affective lability, emotionalism, emotional incontinence, emotion or affective pathology, and emotional dyscontrol. This syndrome has previously been referred to as pseudobulbar affect, given its origin and possible relationship to lesions damaging the neural networks or white matter tracts connecting the frontal lobes, limbic system, brainstem, and cerebellum [22]. However, because additional studies have shown that the majority of these cases of bilateral corticobulbar or corticopontine infarcts are not associated with upper motor neuron lesions, this term has more frequently been replaced by pathological affect [1]. It is crucial that the diagnostician differentiate between the aforementioned neurological disorder and others that may have a similar presentation, such as gelastic or dacrystic epilepsy (ictal laughing and crying, respectively); this emotional lability is associated with a seizure or as part of an aura [23].

The diagnostic criteria for IEED include episodes of involuntary emotional displays, such as laughing or crying, that are attributable to brain disease or injury and deviate from the patient's affective behavior before the onset of brain disease or injury [22]. The episodes are either incongruent with the patient's mood or are congruent but occur with significant exaggeration. Additionally, they may occur without any preceding stimulus. The emotional symptoms cannot be attributable to another neuropsychiatric disorder nor can they be secondary to substance use [22]. Additional clinical observations may also aid in the diagnosis of IEED, such as symptomatology stemming from geographically close cerebral pathology. This definition includes the presence of autonomic changes, as well as pseudobulbar palsy signs, such as increased jaw jerk and gag reflex, dysarthria, dysphagia, and tongue weakness [22]; however, the absence of these associated symptoms must not

exclude this diagnosis as most patients with corticobulbar infarcts will present without them [1]. With the use of the Pathological Laughter and Crying Scale, previous studies have demonstrated the effectiveness of using nortriptyline for 4–6 weeks to treat patients with IEED [24]. Additionally, a double-blind drug trial using citalopram in patients with poststroke IEED also demonstrated a reduction in the number of crying spells by more than 50% [25].

Irritability

Irritability remains one of the predominant neuropsychiatric complications of stroke, with recent studies reporting close to 33% of poststroke patients suffering from irritability [26]. Irritability is one of the most common chief complaints of patients and patient's families when presenting to the neuropsychiatrist. Poststroke irritability is characterized by impatience with situations requiring delays and waiting, flashes of anger, frequent and rapid mood fluctuations, and quarreling.

Cerebrovascular disease is a pathology that not only has serious consequences for the patient himself, but also for members of the family, loved ones, or caretakers of the patient. Certain neuropsychiatric complications of stroke have a greater impact on the patient than the family; however, poststroke irritability oftentimes has a greater impact on those people who interact with the patient than the patient himself. With this consideration, identifying and properly treating poststroke irritability can significantly diminish caregiver burden. One study evaluated the caregiving experience using both the Brain Impairment Behavior Inventory (BIBI) and the companion Brain Impairment Behavior Bother Scale (BIBBS) revealing the three greatest stressors to them as caregivers. The results of this study demonstrated that patient irritability was the greatest stressor for caregivers of stroke survivors [27].

The localization of lesions in patients presenting with poststroke irritability are most commonly within the orbitofrontal lobe, the left cerebral cortex (greater than right), anterior temporal lobes (amygdale), and the limbic system [28]. Risk factors associated with increased rates of poststroke irritability include being aphasic and younger at the occurrence of the stroke. Aphasia increased the irritability rate fourfold, and patients younger than 65 years old had 2.5 times the incidence of poststroke irritability as their older counterparts [26]. Additionally, it has been observed that irritable symptoms of stroke patients usually increase at 1 year poststroke [26]; therefore, if the clinician suspects poststroke irritability, screening should take place at this time. Treatment regimens include mood stabilizers.

Psychosis

In comparison to many of the other neuropsychiatric complications of stroke, psychotic symptoms, such as hallucinations and delusions, are rare. Only five patients followed in a 9-year longitudinal study demonstrated symptoms consistent with poststroke

psychosis [29]. Another study following stroke patients up to 11 years later found a total of eight patients who exhibited psychotic symptoms after right-sided temporoparieto-occipital infarcts [30]. Many of these stroke patients also experienced seizures close to the time at which psychosis was observed. Improvement of their psychotic symptoms was noted after treatment with antiepileptic medications [30].

A frontal lobe syndrome and psychosis have been observed after infarction in the brainstem dopaminergic nuclei, specifically at the ponto-mesencephalic junction. Stereotactic lesion localization on MRI in addition to concordant analysis of regional cerebral blood flow demonstrated that infarction within these nuclei likely has resultant disruption of the ascending dopaminergic projections to the frontal-subcortical circuit components [31]. In addition, a longitudinal study of stroke patients demonstrated that right frontoparietal lesions and subcortical atrophy were significant risk factors for psychosis following stroke given that nonpsychotic stroke survivors did not have these findings [29].

Agitation

Agitation following stroke is observed in approximately 28% of patients who have suffered from a cerebrovascular event. Poststroke agitation manifests primarily by stubbornness (81%), noncompliance, such as with rehabilitation, refusal to cooperate with the patient's caregiver (75%), crying and cursing (75%), and less commonly violence toward objects, such as slamming doors (2%), and never violence toward people [26]. Lesions resulting in poststroke agitation are neuroanatomically confined to the bitemporal lobes and/or the amygdale [28]. The current treatment recommendation includes mood stabilizing agents.

Depression

Given that depression is the most prevalent neuropsychiatric complication of cerebrovascular disease with the greatest quantity of studies and publications, this discussion will devote less to it.

Depression is a frequent complication of stroke, affecting 185,000 stroke survivors in the United States annually. Patients with PSD demonstrate less evidence of recovery from the functional impairments of stroke in comparison to their nondepressed counterparts, and these patients are 3.4 times more likely to die during the first 10 years following stroke [32]. Everson and colleagues [32] found that, in patients with stroke, five or more depressive symptoms at baseline were associated with significantly increased risk of mortality after adjusting for age, sex, ethnicity, education, alcohol consumption, smoking, body mass index, hypertension, and diabetes mellitus. Many patients with PSD also suffer from significant disability and an inability to carry out AODL.

PSD, with documented frequencies of up to 79% [33] of patients who have suffered a cerebrovascular accident, manifests primarily as feelings of uselessness and being a burden on caregivers and family (97%). It also frequently includes feelings of sadness (85%), crying (85%), and less commonly, pessimism and suicidal ideations, both of which are more common in primary depressive disorders [26].

Current evidence suggests that lesions in the basal ganglia or left frontal lobe have a greater association with PSD. Narushima et al. [34] performed a meta-analysis of patients with PSD and noted that there was a significant inverse correlation between severity of depression and distance of the lesion from the frontal pole among 163 patients with left hemispheric stroke, but not among other 106 patients with right hemispheric stroke. PSD is a reflection of failed functioning of critical neural networks, and neurotrophic factors such as brain-derived neurotrophic factor (BDNF) may induce antidepressant effects through neuronal plasticity and recovery of neuronal networks [34]. The most successful treatment regimens for PSD include the use of fluoxetine, followed by nortriptyline, and in some cases, citalopram, trazadone and methylphenidate [11] (Table 1).

Conclusion

This current rendition highlights some of the significant complications resulting from cerebrovascular disease. It brings to attention the importance of correct identification of these conditions to improve the quality of life, as well as the economical and social effects on stroke patients and their families. With greater awareness regarding these diagnoses, hospitalizations and caregiver burden can be decreased, and the proper diagnosis will aid in the appropriate treatment of these conditions.

References

1. Chemerinski E, Levine SR (2006) Neuropsychiatric disorders following vascular brain injury. Mt Sinai J Med 73(7):1006–1014
2. Hadidi N, Treat-Jacobson DJ, Lindquist R (2009) Poststroke depression and functional outcome: a critical review of literature. Heart Lung 38(2):151–162
3. Starkstein SE, Boston J, Robinson RG (1988) Mechanisms of mania after brain injury: 12 case reports and review of the literature. J Nerv Ment Dis 176:87–100
4. Dunne JW, Leedman PJ, Edis RH (1986) Inobvious stroke: a cause of delirium and dementia. Aust N Z J Med 16(6):771–778
5. Braun CMJ, Daigneault R, Gaudelet S (2008) DSMIV symptoms of mania: which ones result more often from right than left hemisphere lesions? Compr Psychiatry 49:441–459
6. Filardi da Rocha F, Horizonte B, Carneiro JG (2008) Poststroke manic symptoms: an unusual neuropsychiatric condition. Rev Bras Psiquiatr 30(2):168–176
7. Leppavuori A, Pohjasvaara T, Vataja R et al (2003) Generalized anxiety disorders three to four months alter ischemic stroke. Cerebrovasc Dis 16:257–264

Table 1 Neuropsychiatric symptoms and lesion localization (modified from [3])

Neuropsychiatric symptoms	Lesion localization	Treatment
Depression	L cerebral cortex, frontal lobe, frontosubcortical circuits, basal ganglia and limbic system	Fluoxetine, followed by nortriptyline, and in some cases, citalopram, trazadone, and methylphenidate
Mania	Anterior region of bilateral hemispheres, R temporal lobe, R caudate nucleus, R subcortical region, R ventral pons, L basal ganglia	Olanzapine, carbamazepine, and valproic acid
Apathy	Frontal lobe, cingulate gyrus, supplemental motor area, amygdala, capsule, insula, caudate nucleus/nuclei, bilateral anterior thalamic nuclei	Stimulating a ntidepressants, i.e., fluoxetine. Stimulating agents, i.e., amphetamine, methylphenidate, selegiline, bupropion. AChE-I
IEED	Bilateral corticobulbar tracts, L frontal cortex	Nortriptyline, citalopram
Psychosis	R hemisphere, especially temporo-parieto-occipital or frontoparietal, and thalamus	Antiepileptics
Agitation	Bitemporal, amygdala	Mood stabilizing agents
Disturbance of sleep–wake cycle	Pons (R > bilateral > L), subcortical regions such as the pyramidal tract and basal ganglia–brainstem axis	Dopamine agonists
Irritability	Orbitofrontal lobe, anterior temporal lobe (amygdala), limbic system, L cerebral cortex	Mood stabilizers
Anxiety	L cerebral hemisphere	Benzidiazepines; in elderly, SSRIs, buspirone
Sexual dysfunction	L basal ganglia, R cerebellum	Poststroke rehabilitation, nonstroke sexual dysfunction meds
Cognitive impairment	Frontal-subcortical circuits, cerebro-cerebellar circuits	Acetylcholinesterase inhibitors, TMS
Fatigue	No specific localization	Stimulating agents

IEED involuntary emotional expression disorder; *AChE-I* acetylcholinesterase inhibitors; *SSRI* selective serotonin uptake inhibitors; *TMS* transcranial magnetic stimulation

8. Dennis M, O'Rrourke S, Lewis S, Sharpe M, Warlow C (2000) Emotional outcomes after stroke: factors associated with poor outcome. J Neurol Neurosurg Psychiatry 68:47–52
9. Starkstein SE, Fedoroff JP, Price TR et al (1993) Apathy following cerebrovascular lesions. Stroke 24:1625–1631
10. Santa N, Sugimori H, Kusuda K et al (2008) Apathy and functional recovery following first-ever stroke. Int J Rehabil Res 31(4):321–326
11. Paranthaman G, Balwin R (2006) Treatment of psychiatric syndromes due to cerebrovascular disease. Int Rev Psychiatry 18(5):453–470
12. Chen JC, Brunner RL, Ren H et al (2008) Sleep duration and ischemic stroke in older women. Stroke 39:315–3192
13. Schuiling WJ, Rinkel GJE, Walchenbach R et al (2005) Disorders of sleep and wake in patients after SAH. Stroke 36:578–582
14. Landau ME, Maldonado JY, Jabbari B (2005) The effects of isolated brainstem lesions on human REM sleep. Sleep Med 6:37–40
15. Lee SJ, Kim JS, Song IU (2009) Poststroke restless legs syndrome and lesion location: anatomical considerations. Mov Disord 24(1):77–84
16. Winward C et al (2009) Fatigue after TIA and minor stroke. Stroke 40(3):757–766
17. Chalder T, Berelowitz G, Pawlikowska T et al (1993) Development of a fatigue scale. J Psychosom Res 37(2):147–153
18. Tamtam Y, Tamtam L, Akil E et al (2008) Post-stroke sexual functioning in first stroke patients. Eur J Neurol 15:660–666
19. Sjogren K, Damber JE, Liliequist B (1983) Sexuality after stroke with hemiplegia: aspects of sexual function. Scand J Rehabil Med 15:55–61
20. Jung J-H, Kam S-C, Choi S-M (2008) Sexual dysfunction in male stroke patients: correlation between brain lesions and sexual function. Urology 71:99–103
21. Saczynski JS, Sigurdsson S, Jonsdottir MK et al (2009) Cerebral infarcts and cognitive performance. Stroke 40:677–682
22. Cummings JL, Arciniegas DB, Brooks BR (2006) Defining and diagnosing involuntary emotional expression disorder. CNS Spectr 11(6 suppl 6):1–7
23. Cummings JL (2007) Involuntary emotional expression disorder: definition, diagnosis and measurement scales. CNS Spectr 12(4 suppl 5):11–16
24. Robinson RG, Parikh RM, Lipsey JR et al (1993) Pathological laughing and crying following stroke: validation of a measurement scale and double-blind treatment study. Am J Psychiatry 150:286–293
25. Andersen G, Verstergaard K, Riis JO et al (1993) Citalopram for post-stroke pathological crying. Lancet 342:837–839
26. Angelelli P, Paolucci S, Bivona U et al (2004) Development of neuropsychiatric symptoms in poststroke patients: a cross-sectional study. Acta Psychiatr Scand 110:55–63
27. Williams A (1994) What bothers caregivers of stroke victims? J Neurosci Nurs 26(3):155–161
28. Luna-Matos M, McGrath H, Gaviria M (2007) Neuropsychiatric manifestations in cerebrovascular diseases. Rev Chil Neuro-Psiquiatr 45(2):129–140
29. Rabins PV, Starkstein SE, Robinson RG (1991) Risk factors for developing atypical (schizophreniform) psychosis following stroke. J Neuropsychiatry Clin Neurosci 3:6–9
30. Levin DN, Finklestein S (1982) Delayed psychosis after right temporoparietal stroke or trauma: relation to epilepsy. Neurology 32:267–273
31. Nishio Y, Ishii K, Kazui H (2007) Frontal-lobe syndrome and psychosis after damage to the brainstem dopaminergic nuclei. J Neurol Sci 260:271–274
32. Everson SA, Robertson RE, Goldberg DE (1998) Depressive symptoms and increased risk of stroke mortality over a 29-year period. Arch Intern Med 158:1133–1138
33. Hadidi N, Treat-Jacobson DJ, Lindquist R (2009) Poststroke depression and functional outcome: a critical review of litreature. Issues Neurol 38(2):151–162
34. Narushima K, Kosier JT, Robinson RG (2003) A reappraisal of PSD, intra- and inter-hemispheric lesion location using meta-analysis. J Neuropsychiatry Clin Neurosci 15:422–430