Post-stroke Neuropsychiatric Problems
İnme Sonrası Nöropsikiyatrik Durumlar

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Abstract
Stroke is the most frequent and significant reason of disability in society. The underlying basic pathophysiological mechanisms of stroke are infarct and hemorrhage. 20% of patients that had a stroke became dependent. Dementia, depression, anxiety disorder, mania, psychosis, pathological emotions, apathy and catastrophic reactions constitute challenging clinical presentations that occur after stroke. In this review, current data about epidemiology, etiology, clinic and treatment of psychopathologies that occur in poststroke period will be discussed.

Keywords: Stroke, clinical presentation, treatment, neuropsychiatry.

Öz
İnme toplumdaki en sık yeti yitimi nedeni olarak göze çarpan bir hastalıktır. İnmenin altında yatan temel patofizyolojik süreçler enfarkt ve hemorajidir. İnme geçiren hastaların %20’si bağımlı hale gelmektedir. Demans, depressyon, anksiyete bozukluğu, mani, psikoz, patolojik emosyonlar, apati ve katastrofik reaksiyon, inme sonrasında klinik tabloyunun zorlu psikiyatrik tabloları oluşturmaktadır. Bu derlemede, inme sonrası dönemde görülen psikopatolojileri epidemiyoloji, etyoloji, klinik ve tedavileri konusunda güncel gelișmeler perspektifinde elde edilen veriler paylaşılacaktır.

Anahtar sözcükler: İnme, klinik görünüm, tedavi, nöropsychiatry.

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STROKE, which is defined as a sudden cessation of the brain blood flow, contributes to psychiatric disability at a great deal, and is the third most common cause of mortality following heart disease and cancer (David et al. 2012). The incidence of stroke, which is common especially in the elderly population, is 2/1000 on an annual scale (Bamford et al. 1988). A total of 750000 stroke cases are reported in the USA every year (Thom et al. 2006). Although the annual incidence is 1-2/1000 between 55-64 years of age, this rate rises up to 2% over 85 years of age (Sadock and Sadock 2007). The prevalence of stroke is 176/100000 in our country. The reported mortality rate, on the other hand, is 24% (Özdemir et al. 2000). However, since the registration system is not reliable in our country, the data on incidence and prevalence rates are not clear. According to Hurwitz and Adams (1972), in an area where 250.000 people live, approximately 150 stroke cases that require continuous care appear on an annual scale. All these data show that stroke is the most common reason of disability in the society (David et al. 2012).

The two main underlying pathological processes of stroke are infarct (ischemia) and hemorrhage. Infarct occurs because of thrombosis or embolism. Although the most common reason of thrombosis is atherosclerosis, the most common reason of cerebral embolism is heart diseases. Infarct is seen 4 times more compared to hemorrhage. Although the survival rate in patients with infarct is 75%; a total of 65% of hemorrhagic patients die within one year’s time following hemorrhage (Bamford et al. 1990). Atherosclerosis, hypertension, heart diseases, diabetes and smoking are among the reasons of stroke (House et al. 1990, Tamam et al. 2008). It was reported in previous studies that there is a stronger relation between hypertension and hemorrhage (Song et al. 2004).

Following stroke, neuropsychiatric conditions appear in most of the cases with different clinical manifestations. It is important to know these neuropsychiatric conditions, which frequently cause that clinicians face challenges in diagnosing and treating the disease. Because, early diagnosis and treatment may be life-saving.

In the present study, the purpose was to review the relation between stroke and neuropsychological conditions, which might appear following stroke, and which are one of the most important health problems in recent years affecting the life quality and the progression of the disease in a negative way, in the light of current literature findings.

**Intracerebral Hemorrhage (IH)**

The mortality rate of IH, which constitutes 10-20% of all the stroke cases, varies between 25% and 60% (Sacco et al. 2009). IH, which is seen more commonly between 60-80 years of age, generally occurs during effort; and headache, vomiting and loss of consciousness are seen more commonly compared to infarct (David et al. 2013). Hypertension (HT), vascular malformations, intracranial tumors, bleeding disorders, anticoagulant therapies, cerebral amyloid angiopathy, vasculitis, hemorrhagic infarcts, traumas and sympathomimetic agents are among the reasons of IH (Bradley et al. 2008). How IH will end up depends on the place, amount and spread of it in the ventricles (Hemphill et al. 2001). It progresses more fatally when compared with the infarct-caused strokes, and disability is more common (An et al. 2017). Definitive diagnosis is made with magnetic resonance imaging (MRI) or computerized brain tomography (CBT) that includes T2 sequences. If stroke emanates from hemorrhage, thrombolytic therapy is contraindicated.
Infarct

A total of 80% of all strokes are caused by infarct; and 50% of ischemic infarcts occur because of large artery atherosclerosis; 25% because of lacunar infarcts, 20% cardiac embolism, and 5% because of more rare causes (Davenport and Dennis 2000). Elderly, male gender, being African American, positive family history, arterial hypertension (AH), transient ischemic attack (TIA), cardiac disease, diabetes mellitus, dyslipidemia, smoking, alcohol use, obesity, use of oral contraceptives, increased fibrinogen/homocysteine levels are among the risk factors for infarct that have been reported in previous studies (Bradley et al. 2008).

In infarcts caused by thrombosis, neurological symptoms generally start in sleep, and proceed in hours-days. The conditions caused by embolism mostly appear during an action, and develop in acute way. Deficits are severe when they first appear; however, they diminish in time. Infarcts have better prognosis compared to bleeding (Keep et al. 2012). Although 20% of the patients recover completely, 20% die in the acute phase, and the rest of them live with disability. Following the embolus, recovery may be faster, and may occur completely due to the collaterals (David et al. 2013).

Prognosis

No matter whether the reason is hemorrhage or infarct, following the stroke, the mortality rate varies between 18 and 50% (Wolfe 2000). Intracerebral hemorrhage and subarachnoid hemorrhage have mortality at higher rates compared to infarct. More than 20% of these patients become dependent on other people at a level that can only meet most of their basic personal needs with help (Wilkinson et al. 1997). Epileptic seizures develop in 3-6% of patients in the early phase, and in 2-4% of patients in the long term. Stroke alone is the most common reason of late-onset epilepsy (Ryvlin et al. 2006). Many psychiatric clinical manifestations appear in addition to neurological deficits following stroke. Each of these manifestations will be reviewed below.

Stroke and Dementia

Stroke is a precursor risk factor for dementia (Pendlebury and Rothwell, 2009). Nowadays, this issue is examined under the name of dementia after stroke or post-stroke dementia (PSD), and consists of vascular dementia (VD), Alzheimer-type dementia (AD), and mixed-form dementia (Cordonnier et al. 2005, Leys et al. 2005). Demographic changes, increasing life expectancy and increasing survival after strokes caused an increase in the number of PSD patients (Leys et al. 2005). Today, the probability of having dementia or stroke at the age of 65 is 1/3 in males, and 1/2 in females (Mijajlovic et al. 2017).

The risk factors for PSD are being over 65 years of age, low education level, being female, having physical diseases and/or cognitive disorders before stroke, the stroke being in hemorrhagic type, the stroke being in the supratentorial region, involving the dominant hemisphere, recurrent stroke development, infection after stroke, delirium, early-stage epileptic seizure development, cortical atrophy in neuroimaging, medial temporal lobe atrophy, and having cerebral small vessel disease (Pasquier et al. 1999, Pendlebury 2009). Age and education level are also important predictor factors (Zhou et al. 2004, Klimkowicz et al. 2006). It was also reported that the number of lesions is
predictive as well (Tamam et al. 2008). Although it was reported in many previous studies that gender is not a predictor, there are several studies reporting that PSD is more frequent in males (Tatemichi et al. 1992, Skoog 2000). The relation between silent brain infarcts, which are frequent in the elderly, and the PSD development has not yet been determined. Ischemic cerebral small vessel diseases, on the other hand, are considered as prodromal pathologies for PSD (Mijajlovic et al. 2017). A total of 30% of stroke patients complain about cognitive impairment following the stroke, and develop dementia within 1 year (Cullen et al. 2007, Öncel et al. 2009). A total of 47.3% of patients who have stroke for the first time experience memory loss within 3 months following the stroke (Jacquin et al. 2014). Stroke increases the risk of developing dementia 4 times more; and the average prevalence is reported as 30% (Barba et al. 2000, Zhou et al. 2004, Tamam et al. 2008). Recurrent strokes increase the PSD risk (Pendlebury 2009).

The data reported in the literature about the relation between the location of the stroke lesion and the development of PSD are not clear. There are several studies reporting that the risk of developing PSD in the lesions that involve the left hemisphere is high (Pohjasvaaara et al. 1998, Desmond et al. 2000); and there are also some authors reporting that PSD might be detected more frequently in bilateral lesions (Tang et al. 2004).

**Clinical Features**

The most common symptoms seen in patients who have PSD are irritability, apathy, insomnia, agitation, intolerance, impatience and emotional lability. Except for these symptoms, emotional incontinence, somatic complaints, restlessness and wandering at nights are also common in these patients. It was emphasized in previous studies that apathy and irritability are important for PSD. It was also reported that depressive symptoms are more frequent compared to AD and it is differential (Cummings et al. 1987).

Multi infarct dementia is characterized by sudden onset. Intellectual functions become worse step-by-step, neurological deficits increase in a fast manner, and some cognitive functions become more disrupted compared to others. Agitation, depression or apathy, visual orientation disorders, and agnosia, which are detected in the early periods following the stroke, may cause misdiagnosis of dementia by clinicians. Especially, amnestic syndrome that is seen in the early phase of posterior cerebral infarcts, recessive-type aphasia that occur following the stroke in the left angular gyrus, and cognitive impairment syndromes accompanied by configuration deficits must be considered by clinicians before diagnosis (Benson and Cummings 1982). Gait disorders may accompany dementia in bilateral thalamic strokes. In addition to dementia symptoms, apathy progressing with excessive sleepiness and vertical vision disorders are observed in bilateral medial thalamic infarctions (Kumral et al. 2001). In anterior thalamic infarcts, on the other hand, a clinical manifestation appears that is characterized with adding irrelevant data to each other together with apathy, amnesia, and perseveration. After paramedian infarcts; however, amnesia, loss of self-activating ability, personality changes, and disinhibited behaviors are also observed. In the inferolateral lesions, impairments are seen in executive functions as well as neglect and aphasia syndromes in posterior lesions (David et al. 2013).
**Biomarkers**

Biomarker studies are carried out for PSD. In cerebrospinal fluid (CSF), the Aβ42 peptide and tau proteins were examined, and it was determined that these markers were not sensitive for VD although they were sensitive for AD (Battistin and Cagnin 2010). Gelatinases are proteins that are associated with myelin destruction. The ischemia that occurs following a stroke induces the A and B Gelatinase. Recent studies show that gelatinase B levels are higher in VD patients at a significant level compared to healthy individuals and AD patients (Adair et al. 2004). There are α antitrypsin, plasminogen activator inhibitor-1 and apolipoprotein H among the CSF markers that are reported to be associated with VD and PSD (Wallin et al. 2012).

**Inflammatory Mediators**

Among the inflammatory mediators that are considered to be associated with PSD, there are erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), IL-6 and IL-12 (Narasimhalu et al. 2015). Recent studies show that there is a relation between ESR and cognitive performance in the period following the stroke. It was determined that patients whose ESRs were high had worse cognitive success (Kliper et al. 2013).

**Neuroimaging**

It was reported that hippocampal atrophy is a strong predictor for PSD (Mehrabian et al. 2015), and especially thalamus, angular gyrus, deep areas of the frontal lobe and left hemisphere lesions are associated with PSD (Grysiewicz and Gorelick 2012).

**Treatment**

The most important way to avoid PSD is to prevent stroke recurrence. In this respect, acetylsalicylic acid provides a decrease at a rate of 21.7-25.1% in nonfatal stroke, MI or mortality. There are studies reporting that blood pressure control with perindopril reduces cognitive decline following the stroke (PROGRESS Collaborative Group 2002). Acetylcholine esterase (ACh) inhibitors and memantine still continue to be the strongest agents to treat dementia and slow down the cellular degeneration (Mijajlovic et al. 2017).

Mead et al. (2013) reported that fluoxetine brought positive cognitive results following the stroke. In addition to all these data, it was also reported that statin use, smoking cessation and good diabetes control are important in the management of the clinical manifestations of PSD (Sadock and Sadock 2007).

**Stroke and Depression**

The lifetime major depression prevalence is 15% (Burvill et al. 1995). It was reported that the rate of depression is between 20-50% in the period following the stroke; and it affects the functional recovery in a negative manner (Aström et al. 1993a). The most common emotional disorder in cerebrovascular diseases is depression (Soyuer and Soyuer 2007). It is determined more frequently in females (Paradiso and Robinson 1998). Although the first three months is the period when the risk of developing depression after stroke (DS) is highest, it was reported that the risk continued for two years more (Robinson and Starkstein 1990). No relation was determined between the type of
stroke and depression (Shimoda and Robinson 1999). The depression occurring in the early period following the stroke increases mortality (Williams et al. 2004).

Although the etiology is not known, possible reasons of DS are the emotional response of the individual to sudden disability and related changes, the change in biochemical balance because of the brain damage, predisposition to depression, and history of depression (Royal College of Physicians 2005). In addition to these, several other factors like the burden brought by coping with physical obstacles, uncertainties about the solutions of problems, becoming dependent on other people, lack of the validity of some previous roles in which the individual felt important and valuable at work and family life, decreasing economic power, and feeling that the individual is worthless also contribute to the development of DS (David et al. 2013).

It is considered that premorbid personality traits are important in DS development, and that struggling, self-sufficient people who do not give up easily can cope with the limitations of stroke better; and anxious people who show depressive reactions in stressful situations are more likely to experience DS (David et al. 2013). It was determined that being socially isolated and being deprived of family support increase the susceptibility to depression (Hackett and Anderson 2005).

There are many studies conducted on the relation between the clinical manifestation and the localization of the lesion to determine the relation between the lesions in the left frontal and right posterior-localized lesions (Starkstein et al. 1987, Shimoda and Robinson 1999). In a study that was conducted with 163 patients and in the meta-analysis of 13 studies, it was determined that there was a reverse correlation between the distance of the lesion from the left frontal pole and the severity of depression (Narushima and Robinson 2003). Today, authors name the pathways that are associated with DS as “frontal-subcortical circuit” or “limbic-cortical-striato-pallidal-thalamic circuit” (Tang et al. 2011). Another parameter that is associated with the presence and severity of depression is the size of the infarct. Vataja et al. (2004) conducted a study with 70 patients, and Nys et al. (2005) conducted another study with 126 patients, and showed that the size of the infarct was significantly greater in the patients who had DS compared to others.

Studies reporting that hyperintensities and silent cerebral infarcts seen in the white matter are associated with late onset DS made us consider that vascular structures might play roles in DS. It was reported that especially the silent lesions that cause damage in the cortico-striato-pallido-thalamo-cortical pathways in time might cause depressive symptoms (Caeiro et al. 2006). One of the mechanisms, which are considered to be responsible for the DS development, is to reduce the bioavailability of serotonin, dopamine and norepinephrine by the lesions that occur as a result of the stroke by preventing the ascending projections that reach frontal cortex by passing through the thalamus and basal ganglia from the midbrain and brain stem. Gao et al. (2008) examined the blood and CSF serotonin levels of 60 DS patients and found that the serotonin levels were low in all samples. Currently, the fact that the selective serotonin reuptake inhibitors (SSRI) and the serotonin noradrenaline reuptake inhibitors (SNRIs) used in DS treatment having clinical efficacy supports this opinion.

The relation between DS and proinflammatory cytokines was also examined by researchers, and it was shown that there is a relation between stroke and interleukin (IL), tumor necrosis factor (TNF) and interférón (IF) (Iadecola and Anrather 2011). In
animal models, the fact that the proinflammatory cytokines like IL-1 and TNF increase infarct and edema in hippocampus and striatum was shown in previous studies support the viewpoint that increased inflammatory response following the stroke causes DS (Caso et al. 2006, Fan et al. 2012). It is known that these cytokines are involved in the control of the synthesis and metabolism of neurotransmitters, and are effective on apoptosis and necrosis mechanisms. IF increases the synthesis and uptake of serotonin (Feng et al. 2014). Aström et al. (1993b) conducted a study with 70 patients, and examined the relation between DS and cortisol. They reported that high cortisol levels after dexamethasone in the 3rd month following the stroke could predict major depression that might occur within three years. Neurogenesis is another topic that is examined by researchers who investigate DS. It was shown in previous studies that hippocampal volume and neurogenesis decreased in depressed patients and animal models, and the antidepressants had effects that caused increases in the hippocampal neurogenesis (Eisch and Petrik 2012). There is also a relation between hippocampal volume and cytokines. Eyre and Baune (2012) reported that systemic TNF-α administration decreased hippocampal cell proliferation and shortened its life. It was shown in previous studies that brain-derived neurotrophic factor (BDNF) played significant roles to maintain neurogenesis and plasticity; and low BDNF levels were associated with DS (Yang et al. 2011, Zhou et al. 2011).

**Clinical Features**

Clinical manifestations of DS are depressive mood, apathy, gaining or losing weight, changes in sleep patterns, fatigue, decreased self-esteem and anhedonia. Depressive mood and apathy are considered to be the core symptoms. In addition to these findings, DS is also related with disrupted learning, disrupted executive and motor functions; and increases mortality and morbidity by affecting stroke rehabilitation adversely (Loubinoux et al. 2012, Quaranta et al. 2012). Spaletta et al. (2005) conducted a study and reported that depressive mood, loss of desire-interest, fatigue, insomnia, psychomotor retardation and agitation were more prevalent in DS patients. The symptoms that are in the foreground may change over time in DS. Although autonomic and vegetative symptoms might appear in earlier stages, vegetative and psychological symptoms might be detected together in further stages (Paradiso and Robinson 1998). If DS is with early onset, it was reported that lesion volume is larger and vegetative symptoms are more prevalent (Tateno et al. 2002). Unlike what is considered, no relations were determined between the depressive mood severity and motor deficits (Andersen and Vestergaard 1994). It was reported that subcortical basal ganglion and brain stem lesion depressions lasted shorter than the depressions that stem from cortical lesion (Starkstein et al. 1988).

DS is differentiated from the depression that develops after myocardial infarct or spinal cord trauma with anxiety symptoms being detected more (Castillo et al. 1993, Dilbaz et al. 1994). In addition, more reduction is observed in cognitive functions. It should not be forgotten that DS increases mortality (Morris et al. 1990).

**Treatment**

In the publications that were released in the first period about the DS treatment, conflicting results were obtained on the efficacy of the drugs. The reason for this might be
the inability to complete the study by patients due to tricyclic agents that had more anticholinergic side effects because the patient were old. With the use of SSRI and SNRI group drugs, the success in the treatment in DS increased, and this group was used more often. SSRIs still continue to be the first choice in the treatment (Gainotti et al. 2001).

In a double-blind placebo study conducted with 66 patients, although the citalopram response rate was reported as 59%, this rate was 28% in placebo (Andersen et al. 1994a). In addition, Wang et al. (2008) showed that the proliferation and survival of neurons increased with citalopram in rat DS models. Bilge et al. (2008) reported that 20 mg/day citalopram that was administered in depression patients following stroke provided a clinical recovery in patients, and increased the functional recovery rates of the patients. Robinson et al. (2000) conducted a placebo-controlled study and compared the efficacy of nortriptyline and fluoxetine in DS, and reported that nortriptyline ensured more reduction in Hamilton Depression Scale (HAM-D) scores at the end of 12 weeks, and there were no differences between fluoxetine and placebo.

Escitalopram is preferred more because it is an effective molecule and has less drug-drug interaction and low side effects. Havle et al. (2010) conducted a study with 35 DS patients, and obtained a significant reduction in depressive symptoms with escitalopram (10mg/day) at the end of the 3rd month. In a study in which the results of 16 randomized controlled studies were examined, it was determined that the response rate to antidepressants was 65%, and the response rate to the placebo was 44% (Chen et al. 2006). In a study that was conducted with 20 patients who were diagnosed with DS, it was reported that sertraline was effective and tolerated well (Spalletta and Caltagirone 2003). Zifko et al. (2002) conducted a study with 267 DS patients, and reported that there were decreases in the depression scores of 252 patients with sertraline; however, there were no changes in 10 patients, and 5 patients left the study because their symptoms were deteriorated.

**Stroke and Anxiety Disorders**

Anxiety is a symptom that is observed frequently in the acute and chronic period of stroke (Lincoln et al. 2013). Studies report that 30% of stroke patients experience anxiety at varying severities (Watanabe 2005, Gilworth et al. 2009). Post-stroke anxiety disorder (PSAD) is observed more frequently in young patients (Broomfield et al. 2015). It is already known that anxiety which is experienced in post-stroke period, is independent from gender and depressive symptoms, and stems from worries like whether stroke will strike again, whether the patient will work again, and whether she/he will maintain his/her social activities; and is related to life quality (Tang et al. 2013). It was determined in previous studies that all anxiety types were observed in the period following the stroke, and these affected the life quality negatively (Knapp et al. 2017).

When the literature is examined, it is seen that there are no adequate studies conducted on PSAD. The reason of this might be that researchers are focused more on depression, and anxiety might be overlooked due to high comorbidity levels. In addition, further age and decreasing speech ability might make it difficult to detect PSAD (Van Rijswijik et al. 2009). According to a meta-analysis study which examined 37 studies, PSAD was detected in 29.3% of the patients in the first year following the
stroke, and in 37.7% in the first 2 weeks (Rafsten et al. 2018). Major and minor depression frequently accompany PSAD (Dilbaz 2001). It was determined that depression was more serious and lasted longer when anxiety accompanied as comorbidity (Shimoda and Robinson 1998). In another study, generalized anxiety disorder was determined in 28% of 80 acute stroke patients; major depression was determined in 55% of these patients (Sadock and Sadock 2004).

The number of lesion-location studies conducted for PSAD is relatively small when the studies conducted on DS are considered. There are studies which report that there is a relation with left cortical lesions in DS and PSAD together, and a relation with right hemisphere lesions when there is only PSAD (Castillo et al. 1993, Shimoda and Robinson 1998). It is required that there are at least three of the following criteria in the diagnosis of PSAD; restlessness, early tiredness, difficulty in concentration, irritability, sleep disorder and muscle tension. The alcohol use history is significantly higher in generalized anxiety disorder in acute stroke patients (Sadock and Sadock 2004).

Chun et al. (2018a) conducted a study in which they investigated PSAD, and examined the anxiety under two titles as phobic and generalized; and determined that the phobic type was more dominant in stroke patients. It was determined that stroke patients avoided agoraphobia-related situations (going out alone, going to crowded places, using public transport, spending effort, avoiding sexual activity, experiencing stroke again, falling down); and the most dominant one among these was having another stroke again (Chun et al. 2018b). The likelihood of PSAD being detected in adolescents, women and those who have a history of anxiety is high.

**Treatment**

Paroxetine and buspirone are the two influential agents that are well-tolerated in PSAD treatment. Paroxetine and psychotherapy combination did not yield a significant difference (Knapp et al. 2017). Mikami et al. (2014) conducted a placebo-controlled study, and determined that both the escitalopram and problem-solving therapy were beneficial in avoiding PSAD. Rao et al. (2012) conducted a 16-week pilot study, and started sertraline for 4 patients who had PSAD. At the end of the study they reported that there were decreases in the complaints of three patients, and one patient left the study because of increased anxiety. Robinson et al. (2000) conducted a study and compared nortriptyline and placebo. They determined that there were significant decreases in the Hamilton Anxiety Scale (HAM-A) scores. Clinicians must be careful in terms of sedation, ataxia, disinhibition and confusion when they are using benzodiazepines in ISAB (Dilbaz 2001).

**Stroke and Mania**

Post-stroke mania (PSM) is not a common clinical manifestation. Robinson et al. (1988) reported only 2 mania cases in 500 stroke patients. There are no epidemiological studies showing the incidence and prevalence of PSM. The mania, which occurs following a brain injury is called secondary mania, which might be metabolic, pharmacological and neurological (Krauthammer and Klerman 1978). Unlike the post stroke manifestations, manic symptoms develop in the first year in 10% of patients who experience closed-head traumas (Starkstein and Robinson 1997). The reason for the amount
of PSM being low is that the orbitofrontal and basotemporal areas, which are the areas that are frequently damaged in traumas, are rarely affected in a stroke (Dilbaz 2001).

It is considered that PSM is triggered by the damage of right hemisphere structures, which have connections with the limbic system. Especially the loss of the inhibitory impact caused by this region together with orbitofrontal cortex in the basotemporal cortex damages that are associated with secondary sensory and multimodal association regions and the limbic and paralimbic regions cause disinhibition symptoms (Starkstein and Robinson 2000). Although the data on the relation between right hemisphere lesions and mania are dominant in the literature, there are also some mania case reports on left hemisphere lesions (Turecki et al. 1993, Liu et al. 1996). The sudden disruption of the neuronal synaptic functions, blood flow and metabolism following an acute damage to the central nervous system for any reason is called diaschisis. Diaschisis is a process that occurs depending on a focal damage and it is reversible (Meyer et al. 1993). McGilchrist et al. (1993) reported a case with bipolar disorder following thalamic infarct. It was reported that thalamic infarcts might cause secondary mania by leading to metabolic dysfunctions by diaschisis mechanism and in the frontal lobes. The fact that mania does not develop in every patient who has right hemisphere lesion made clinicians consider that there should be some other risk factors in such patients. These are familial genetic load in affective diseases, subcortical atrophy and the damage in right hemisphere limbic region (Santos et al. 2011).

Clinical Features

Secondary mania appear at further ages compared to primary mania. Mania might start immediately after the stroke or after months-years (Das and Khanna 1993). Neurological diseases are seen twice as much in late-onset bipolar disorders (Tohen et al. 1994). Although PSM symptoms show similarities with primary mania, irritability, aggression and agitation are more dominant in the clinical manifestation (Santos et al. 2011).

Treatment

The treatment of PSM is similar to that of the primary mania. However, the treatment is difficult and the response to treatment is slow (Evans et al. 1995). Lithium is the most preferred one among the mood stabilizers. Using lithium in elderly population might cause problems because of the fact that non-steroidal anti-inflammatory drugs that are used often by this patient group might reduce the lithium clearance, and cause neurological side effects, and because lithium can cause hypothyroidism in the elderly more easily. Using valproic acid (if there is no hepatic failure) or carbamazepine (if there is epilepsy) in patients who have secondary mania will be more appropriate. There are not adequate studies conducted on topiramate and lamotrigine. Risperidone, quetiapine, olanzapine and aripiprazole might be used as antipsychotics (Evans 2006, Brooks and Hoblyn 2005). Antipsychotic agents might be used for agitation in elderly patients. In addition to this, lorazepam might be a proper preference as it is metabolized through phase II glucuronidation, and its effects are not long-lasting.

Stroke and Psychosis

Psychosis that develops after stroke has been given different names throughout history like “agitated delirium, acute atypical psychosis, peduncular hallucinosis, oscillation
hallucination, acute organic psychosis” (Dilbaz 2001). The incidence of post-stroke psychosis (PSP) varies between 1% and 5.3%. In a study in which 360 cases were examined, delusions were detected in 15 patients (Kumral and Öztürk 2004). In a large-scale cohort study, the cumulative psychosis incidence was determined as 6.7% in patients who were followed-up for 12 years as of the first stroke attack (Almeida and Xiao 2007).

To explain the reason why PSP is so rare, it is suggested that lesions must exist in more than one area for the delusions to be noticeable in clinical terms (Devine et al. 2014). In addition, it was reported that cerebral atrophy -especially in frontal horns and trunk of the lateral ventricle, i.e. subcortical atrophy- facilitates the occurrence of PSP (Rabins et al. 1991). There are also several other studies reporting that the manifestation of psychosis develops more often in the right inferior frontal gyrus damages. In addition, it was also reported that signal disorders that might appear in right inferior frontal gyrus might also create predisposition to psychosis in healthy people (Corlett et al. 2007). In addition, it was reported that the presence of schizotypal characteristics in the history of patients might cause susceptibility to PSP (Linscott and van Os 2010). When the literature is examined, it is seen that particularly the lesions in the right temporoparietooccipital region have high risks for PSP (Starkstein et al. 1992, Edwards-Lee and Cummings 2000). The right hemisphere lesions are considered as a risk factor for PSP (Rabins et al. 1991).

It was reported in the literature that the seizures stemming from lesions increased the probability of PSP development as well as anatomical localizations (Dilbaz 2001). In a study, it was reported that in 7 of the 8 right temporoparietooccipital stroke or traumatic injury cases there were psychosis and seizures (Levine and Finklestein 1982). The hypothesis claiming that the electrical activity that is caused by the lesion plays roles in psychosis development was suggested after this association was detected (Mishra and Hastak 2008). Symptoms vary according to the location of the lesion in PSP. It was reported that psychotic symptoms usually start in the first week after stroke. There are several studies, which report that PSP starting after the first week might be associated with epilepsy (Barboza et al. 2013).

Treatment

PSP responds well to antipsychotics. There is no treatment protocol that has been established for PSP treatment. Treatment suggestions are limited with case reports. There are case reports in the literature reporting that clozapine and valproic acid (Almeida et al. 2011) risperidone (Ferreira et al. 2017), fluvoxamine and chlorpromazine (Rocha et al. 2014), and fluoxetine and risperidone (Duggal 2005) yielded positive results.

Post-stroke Pathological Emotions

It is a clinical condition that is characterized with uncontrollable laughing/crying episodes, which might appear several times a day, which result from damage to the areas involved in emotional regulation. Laughing/crying episodes occur in an independent manner from mood and social context, and causes social isolation and decreased life quality because of the shame it causes in the individual (Ahmed and Simmons 2013). It is also called under many different names like post-stroke pathological emotions (PE),
emotionalism, pseudobulbar emotions, emotional lability, emotional incontinence, and post-stroke labile emotion (Andersen et al. 1994b). Although this clinical manifestation is not represented by any of these names in DSM-5, it may be defined as “Possible dominant vascular neurocognitive disorder progressing with behavior disorders (F01.51)”. PE might appear after dementia, stroke, traumatic brain damage, amyotrophic lateral sclerosis, multiple sclerosis, epilepsy, posterior fossa tumors, vascular malformations and Parkinson’s disease (Tateno et al. 2004).

Pathophysiological process has not yet been understood fully. Although the response of PE to antidepressants makes clinicians consider that it is associated with depression, studies that were conducted to determine this association could not detect a symptomatic or diagnostic relation between PE and depression (Robinson et al. 1993, Feinstein et al. 1997, Petracca et al. 2009). The hypothesis that is most widely accepted is that the dysfunction of cortico-pontine-cerebellar circuit causes PE (Parvizi et al. 2009). The fact that this syndrome develops following the damage to the hemisphere and to the raphe nucleus itself made clinicians consider that PE was caused by serotonergic system dysfunction (Andersen et al. 1994b). The SSRIs being efficient in treatment strengthens this hypothesis (Brown et al. 1998, Burns et al. 1999). The rate of PE in the first year following the stroke is 15-20%. PE is more frequent in hemorrhagic stroke compared to ischemic stroke (Robinson 1998). Crying is seen more commonly than laughing. In patients who have bilateral pontine lesions, crying periods are more frequent. The PE frequency has increased in patients who experience depression after stroke.

**Treatment**

Evidence is increasing for the efficacy of SSRIs, which are used frequently in PE treatment. There are a great number of studies conducted on the efficacy of fluoxetine (Brown et al. 1998), citalopram (Andersen et al. 1994b), paroxetine (Derex et al. 1997) and sertraline (Burns et al. 1999) in PE. It is possible to claim that citalopram and escitalopram are the most selective and are one step ahead compared to other SSRIs because of the serotonergic system dysfunction that is emphasized in pathophysiological processes (Hiemke and Hartter 2000). In addition, there are studies reporting that amitriptyline, lamotrigine and mirtazapine are also effective in PE treatment (Schiffer et al. 1985, Ramasubbu 2003, Kim et al. 2005). Dextromethorphan/quinidine, which have antiglutamatergic and serotonergic effects, have been used recently in PE treatment. Randomized controlled trials that were conducted on this combination show that it has significant efficacy compared with placebo (Pioro et al. 2010, Ahmed and Simmons 2013).

**Apathy**

Apathy is the decrease of targeted actions at significant levels because of motivation loss. The cognitive findings are lack of interest, inadequacy in planning the future. The emotional findings are superficial affect and indifference. Simultaneous decreases are observed in all of the purposeful thought, behavioral and emotional expression (Marin 1991).

The rate of apathy in 80 cases with a single stroke lesion was determined as 11% (Robinson et al. 1984). According to Jorge et al. (2010), the frequency of developing...
apathy following a stroke is between 20 and 25%. Apathy is seen more frequently in elderly patients (Dilbaz 2001). Starkstein et al. (1993a) conducted a study with 80 patients who had stroke, and determined the rate of detecting apathy as 22.5%. According to the study results, post-stroke apathy is associated significantly with further age, cognitive disruption, deterioration in daily life activities, major depression and internal capsule back leg lesions. Brodaty et al. (2005) conducted a study with 167 patients who had ischemic stroke and a control group consisting of 109 people, and detected apathy in 26.7% of stroke patients, and in 5.4% in the control group; however, they failed to detect a correlation between apathy and depression. They also failed in detecting any associations between apathy and the type of the stroke, its location, volume and severity. Apathy is seen in 60% of the conditions that affect the cerebral cortex, and in 40% of the events that affect the subcortical regions (Reekum et al. 2005). Apathy is observed especially in the medial frontal cortex lesions, and in dorsolateral frontal cortex, anterior and medial nucleus of the thalamus, and in striatum and amygdala lesions (Dufy and Kant 1997).

**Treatment**

SSRIs, nortriptyline, apomorphine, amphetamine, methylphenidate and bromocriptine are used in the treatment of apathy. In addition to these treatments, Whyte et al. (2008) reported in their studies, which investigated the efficacy of donepezil and galantamine in stroke patients that the apathy rates of the patients who used donepezil decreased at a significant level. Another agent that promises hope is nefiracetam in apathy treatment. Nefiracetam is a new cyclic GABA compound, which has been shown to increase aminergic, glutamatergic and cholinergic neurotransmission by stimulating the $\beta_2\beta_2$-type neuronal nicotinic acetylcholine receptors (Jorge et al. 2010). Robinson et al. (2008) reported that nefiracetam was effective at a rate of 900mg/day in apathy that was associated with post-stroke depression.

**Catastrophic Reaction**

This term, which was first used by Goldstein, is used to describe aggressive behavior, anxiety, crying, swearing, rejection, and sometimes, compensatory boasting conditions (Goldstein 1948). It was claimed that it stemmed from the failure of the organism in coping with the physical and cognitive deficits it faces. This clinical manifestation might be expressed in DSM-5 with the diagnosis “Possible dominant vascular neurocognitive disorder progressing with behavior disorders (F01.51).

Catastrophic reaction (CR) is seen more frequently in the left hemisphere lesions; and the rate of psychiatric disorders in the familial and personal history of patients with CR is more (Gainotti 1972). Depression was diagnosed in 75% of CR patients. Its frequency after acute stroke was determined as 19-20%. Basal ganglion involvement and anterior side lesion located in the subcortical region are more common in such patients. Subcortical damage causes that the emotional expression is released in an unlimited manner by preventing the inhibitor inputs of the limbic areas of the cortex. No differences were detected in terms of CR in aphasic and nonaphasic patients. No effective treatment modalities have been reported (Starkstein et al. 1993b).
Conclusion

It is believed that stroke, which is currently the most important cause of social disability, will remain in this form in the future because of the increasing life expectancy in humans. Although developments have been reported in the treatment of stroke, it is inevitable that the number of patients, who are in need of constant care, will increase with the effect of continuously increasing population. One of the consequences that are inevitable brought with this condition is the psychiatric symptoms caused by stroke. Dementia, depression, anxiety disorder, mania, psychosis, pathological emotions, apathy and CR are the psychopathology group which clinicians will face in the polyclinic, service or intensive care units after strokes. When the literature was examined, it was seen that there were few studies especially on psychopathologies in the post-stroke period. The increase in our knowledge in terms of epidemiological, etiological, pathogenesis and treatment of these psychopathologies will help us to make necessary regulations in treatment by examining the risk factors specifically for patients, and to administer the correct treatment agents at the correct time. In this way, the life and working qualities of patients, their relatives and clinicians will increase.

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