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Brief mini review

COMORBIDITY FROM A NEUROPSYCHIATRIC PERSPECTIVE

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SUMMARY

Comorbidity in neurology and psychiatry involves the onset of a mental illness with the simultaneous presence of a neurological disorder or other illness. The degree of comorbidity of mental and neurological disorders is unexpectedly high. In addition to the direct connection and simultaneous occurrence of mental and neurological illness, the indirect impact of mental illness on the occurrence of neurological problems is even more significant. This link is realized through the influence of mental illness on risk factors for the development of cerebrovascular and cardiovascular diseases. Their incidence is higher in the psychiatric population than in the general population. Numerous studies have confirmed that risk factors for cerebrovascular disease (hypertension, hyperlipidemia, diabetes mellitus, etc.) are more common among patients with mental disorders than in the general population. Also, research shows that patients with mental disorders are less frequently controlled, have less control over risk factors, and that numerous comorbidities are detected later or remain undetected. Given that cerebrovascular and cardiovascular diseases represent one of the most important public health and socioeconomic problems of today, both in the world and in Croatia, this problem should not remain in the shadow.

Key words: *comorbidity - neurological diseases - mental disorders – epidemiology - somatic disorders*

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COMORBIDITIES IN NEUROLOGICAL DISEASES

More and more research is suggesting the simultaneous occurrence of mental and somatic disorders (Cimpean 2005, El-Mallakh 2006, Barnett 2012). The nature of the relationship between mental and somatic conditions has not been fully elucidated, due to numerous mechanisms and interactions. While the occurrence of mental disorders in patients with somatic diseases can be well explained, understanding the mechanisms involved in the development of increased somatic morbidity in psychiatric patients is significantly more complex.

The comorbidity of mental and somatic disorders is an extremely important area of daily work, emphasizing the need for a holistic approach to patients. The relationship between the mental and the somatic is two-way, thus creating a platform for collaboration among different specialists.

People with serious mental disorders have higher rates of morbidity and mortality for cardiovascular and cerebrovascular diseases, diabetes, respiratory diseases, infectious diseases and certain cancers than the general population (Scott 2016). Depression and anxiety are related to obesity, asthma and renal disease (Cohen 2015, Ortega 2001, Goodwin 2003). According to the literature, half of psychiatric patients have known comorbidity, 35% have an undiagnosed disease, and 20% have a health problem that can be a cause of a mental disorder.

STROKE

One of the most common neuropsychiatric complications of stroke is depression. The prevalence rates are over 22% for major depressive disorders and about 20% for minor depressive disorders in rehabilitation centers. There is an association between a brain region affected by a stroke and the development of depression after a stroke. Physical impairment is also significantly associated with an increased incidence of depression. An Italian study showed a depression rate of 27%, anxiety disorder in 12% of patients, and personality disorder in 10% of patients. Long-term depression is present in patients who have a generalized anxiety disorder in addition to depression. The combination of these diseases leads to more severe mental and social functioning. Also, the outcome after a stroke can be significantly improved if psychiatric disorders are identified and treated on time.

Studies have shown that carotid revascularization after stroke is worse in patients with mental illness, especially those with schizophrenia or psychosis, depression, addiction or multiple psychiatric diagnoses (Bongiorno 2019, Chaturvedi 2017).

COMORBIDITY IN DISEASES THAT PRESENT AN INCREASED RISK FOR CEREBROVASCULAR COMPLICATIONS

Among the most common comorbidities in patients with mental disorders are obesity (24%), hypertension (22%), diabetes (12%), and chronic obstructive pulmonary disease (10%). Studies also suggest the presence of metabolic, gastrointestinal, pulmonary, cardiovascular, cerebrovascular, and neurological diseases, as diseases that often occur among psychiatric patients (Ryu 2016, Miller 2006, Hartz 2014, Koran 2002).

Studies show that most serious psychiatric disorders are associated with a high mortality rate (Liu 2017).

This can sometimes be related to an existing psychiatric problem. Unhealthy lifestyles, such as smoking or poor nutrition, lack of physical activity, drug use, and excessive alcohol consumption, and side effects of psychotropic drugs, all contribute to the occurrence of comorbidity (Morović 2019). Although the relationship between unhealthy lifestyle habits, psychotropic medications, and increased mortality rates among patients with psychiatric disorders is well known, scientific evidence is lacking (Rasanen 2007). Also, it has not been sufficiently investigated whether there are differences between ethnic groups (Scott 2008).

MIGRAINE

Migraine is a common disabling neurological disorder with a wide range of medical and psychiatric comorbidities. Studies have shown that psychiatric comorbidities such as mood disorders and anxiety are more common in people with chronic migraines than those with episodic migraines. Research has also shown that psychiatric comorbidities may be a risk factor for chronic migraine headaches, like transition from episodic to chronic migraine. It is important to identify and appropriately treat comorbidities as they significantly contribute to the reduction of health-related quality of life and treatment outcomes (Demarin 2020).

Depressive symptoms were identified in almost 50% of the migraine population compared with 17% in the non-migraine population. A Detroit study found similar results. Depression was diagnosed in 40% of people with migraines and 16% in the control group. Increased frequency of migraine headaches is associated with higher rates of depression.

Generalized anxiety disorder is twice as common in people with migraine. A Swiss study on young adults found that the rate of generalized anxiety disorder is even up to five times more common in people with migraine headaches than those without headache. Post-traumatic stress disorder is more common in people with migraines than the general population. Post-traumatic stress disorder is associated with abuse, neglect, exposure to violence, and other traumatic life events. Several studies have shown a link between childhood bad circumstances and the onset of migraines (Buse 2012, Chaturvedi 2017).

DEPRESSION AND NEUROLOGICAL DISEASES

In patients with affective disorder, there is a prevalence of 8% for men and 13% for women to develop depressive episodes at 12 months. Depression is associated with comorbidity with many disease categories, most commonly occurring in individuals with gastrointestinal disease, stroke, musculoskeletal disease, Parkinson's disease, respiratory disease, and obesity (Nuyen 2006, Kessler 2005). Mental disorders such as depression can lead to over-consumption of food and therefore obesity, thereby increasing the risk of diabetes and cardiovascular disease. On the other hand, chronic diseases affect the onset of depression. Diabetes mellitus is a common health disorder that causes depression. Neoplasms are often associated with depression, although their relationship is not fully understood. Immunosuppression is now associated with depression, resulting in a possible increase in cancer risk in susceptible individuals (Leucht 2006, Jung 1999).

Howard's study found that the most common physical conditions that accompany depression are back and spine problems (66%), arthritis (65%), indigestion (63%), and migraines (58%) (Howard 2007). Also mentioned are high rates of hypertension in patients with depression, which affects their overall risk of cerebrovascular and cardiovascular disease. Studies also show that patients with depression, with the presence of chronic physical disorders, have a harder time adhering to treatment programs and are less likely to engage in activities and care for their health (Carney 2002, Grimsrud 2009, Liddy 2014).

EPILEPSY

For years epilepsy has been considered a central nervous system disorder manifested only by the onset of seizures, and its treatment has been focused at preventing recurrent seizures. Over the last twenty years, we have learned that seizures are just one manifestation of epilepsy, and that it is accompanied by a large number of psychiatric comorbidities. Almost every third patient with epilepsy has some psychiatric comorbidity (Demarin 2020).

Today we know that psychiatric comorbidity and epilepsy are in a complex relationship. Not only do people with epilepsy have an increased risk of psychiatric disorder, but people with primary psychiatric disorder have an increased risk of developing epilepsy. Epidemiological data suggest that there is a two-way relationship between some psychiatric illnesses and epilepsy, including mood disorders and anxiety, depression, and psychosis. This is not to say that epilepsy causes a psychiatric disorder, and vice versa, but it does suggest that there are common pathogenic mechanisms in epilepsy and psychiatric disorders. Very often a psychiatric disorder occurs before the onset of the first seizure and can have a negative impact on the course and treatment of future seizures.

Psychiatric comorbidities can affect the course and management of the disease at several levels, including:

- A history of mood disorders prior to epilepsy may be associated with a higher risk of treatment-resistant epilepsy.
- A positive trait and / or family history is associated with an increased risk of non-psychiatric and psychiatric adverse events associated with antiepileptic therapy.

- A current and/or past history of a positive mood disorder can facilitate the development of seizures associated with stressful situations.

Studies have shown the negative impact of a positive psychiatric history on patients with newly diagnosed epilepsy on the course and management of the disease, as well as on the recurrence of psychiatric comorbidities and / or other complications. The examination of personal and family psychiatric history should be part of the patient's initial evaluation given that it can play a significant role in the choice of antiepileptic drugs and the further course of treatment (Kanner 2017, Chaturvedi 2017).

BIPOLAR AFFECTIVE DISORDER

People with bipolar disorder also show higher rates of comorbidity with physical illness. (Kupfer 2005) The most common are hypertension, hyperlipidemia, and hepatitis C. In nearly 20% of patients with bipolar disorder, type II diabetes occurs, which is more than the general population. Again, comorbidities include hypertension, cardiovascular disease, asthma, diabetes and HIV. The Howard study also showed comorbidities with the highest prevalence here, with neck and spine problems 66%, arthritis 65%, digestive problems 62% and migraines 57%. The worrisome part is that patients with bipolar disorder who have at least one of the comorbidities, this comorbidity is not adequately treated (Kilbourne 2005, Beyer 2005, Howard 2007).

Anxiety disorders are often accompanied by different physical conditions. Especially when anxiety disorder occurs with depression, physical problems are more pronounced than when these conditions occur without comorbidity. The prevalence of respiratory disease in these patients is estimated to be as high as 47%. There may be overlapping symptoms between the two disorders. The high prevalence of hypertension, diabetes and cardiovascular disease is also evident in these patients (Scott 2007, Ortega 2003).

MULTIPLE SCLEROSIS

Multiple sclerosis is an autoimmune disease in which inflammatory demyelinating changes in the central nervous system occur. Psychiatric symptoms in patients with multiple sclerosis, although common, often remain overlooked. Changes in mood, personality and cognitive functioning are among the most common symptoms, with patients and their families rarely getting help in the area. Studies show that the prevalence of psychiatric comorbidities is high at the time of diagnosis of multiple sclerosis, and further increases during illness. Among the most common diseases are depression, anxiety and bipolar disorder.

Psychiatric disorders in these patients have a major impact on various aspects of the lives of patients with multiple sclerosis. The prevalence of psychiatric comorbidities is high at the time of diagnosis, but continues to increase throughout the disease. Studies show that more than 10% of patients have some type of cognitive impairment at the time of diagnosis. People with major disabilities also showed poorer results on cognitive tests. Almost half of the patients had some sort of physiological distress. Also, the study found that distress was increasing as physical deterioration occurred. A third of patients suffer from anxiety from the very beginning of the disease. This phenomenon is very pronounced in young patients with minor physical disabilities. Some studies, such as England, show anxiety rates of up to 50%. A number of patients have severe depressive symptoms, and their occurrence is also related to the level of physical disability. Different studies show different results so that the percentage of patients with depressive symptoms varies from 25 to 70%, depending on the study. A certain percentage of patients, about 15%, become alcohol dependent, predominantly men.

Psychiatric illnesses often accompany patients with multiple sclerosis, further impairing their quality of life and exacerbating distress. Depression is the most common symptom, followed by anxiety. Also, a larger neurological deficit is accompanied by a more severe psychiatric disorder. In patients with multiple sclerosis, psychiatric comorbidity needs to be addressed in order to be able to intervene promptly (Panda 2018).

ANXIETY

Anxiety disorders are more commonly associated with gastrointestinal problems and endocrine disorders or arthritis, than the general population. Diagnosis of post-traumatic stress disorder increases the likelihood of endocrine disorder, diabetes, obesity, and hyperlipidemia (Johannessen 2006, David 2004).

Panic disorders are closely related to hypertension, irritable bowel, migraine and respiratory and cardiovascular disease. Many of these disorders lead to the manifestation of panic symptoms, while anxiety symptoms can worsen the physical condition. Today, a strong link between mitral valvular prolapse, which is present in about 30 to 50% of patients with panic disorder, has been demonstrated. Panic disorders are very often misdiagnosed in everyday practice (Simon 2005, Lung 2008).

Generalized anxiety disorder and hyperthyroidism are common in the general population. In everyday work, differential diagnosis is sometimes difficult. Treatment with thyroid function has shown that patients with anxiety disorder do not have thyroid dysfunction or, if dysfunction is present, it is usually minimal (Simon 2002).

In anxious individuals, manifestations of health-related behaviors such as smoking or drug use are associated with increased rates of morbidity and mortality (Mykletun 2007).

Schizophrenia is associated with numerous somatic conditions and is often referred to as a "life-threatening disease". Almost half of schizophrenia patients have some physical comorbidity (Cimpean 2005, El-Mallakh 2006, Barnett 2012). Diabetes mellitus, cardiovascular disease, hypertension, osteoporosis, respiratory disease, obesity, and metabolic syndrome are just some of the common diseases that accompany it. Hepatitis virus C infection and HIV were found in about 4-22% of these patients. Also, patients with schizophrenia have a reduced sense of pain (Heiskanen 2003, Cournos 2005, Nasrallah 2005).

High rates of physical comorbidities are related to several factors. The use of common antipsychotics is associated with a high prevalence of metabolic syndrome. Unhealthy lifestyle habits in psychiatric patients such as poor nutrition, lack of physical activity and smoking have an increased incidence of diabetes mellitus, obesity, cardiovascular disease, lung cancer, emphysema and bronchitis.

COVID-19

Viral infections of the respiratory tract can have multisystemic effects, including on the central nervous system (CNS), and thus may precipitate a spectrum of psychiatric and neurological disorders. Some patients with covid-19 are now known to develop various CNS abnormalities with potentially serious and long term consequences, including stroke and isolated psychiatric syndromes (Butler 2020, Budincevic 2020). Additional biological mechanisms, including autoimmunity, may be relevant to neurologic and psychiatric disorders. The relative contributions of these mechanisms to neuropsychiatric complications remain largely unknown.

Neuropsychiatric symptoms, particularly delirium, were common in previous coronavirus outbreaks and so far, covid-19 seems to follow a similar pattern: delirium is the most common acute neuropsychiatric syndrome and may be the sole presenting feature of covid-19 in older adults and those with dementia. Delirium is associated with poorer outcomes and is especially prevalent among patients requiring intensive care, where cognitive and behavioural abnormalities have been reported in one third of patients after discharge (Helms 2020).

Screening for delirium should be considered in acute cases, particularly in older adults or those with pre-existing dementia, along with close monitoring for longer term adverse outcomes such as cognitive impairment. Efforts should also be made to identify patients with alterations in mental state that are not explained by delirium, as they may need more advanced diagnostic and therapeutic approaches.

During previous coronavirus pandemics, low mood and anxiety were common in the acute phase of infection (with psychosis and catatonia in a minority), and in one study of COVID-19 patients admitted with acute respiratory distress syndrome, fatigue persisted after discharge in around one fifth (Rogers 2020). High rates of anxiety, depression, and post-traumatic stress disorder have been reported in people who recover after hospital admission for COVID-19, but it is still too early to measure the full effect of long term complications. Some patients treated in hospital for severe COVID-19 experience disabling fatigue and cognitive difficulties (Zhou 2020) after discharge.

Concerns regarding potential neurological complications of COVID-19 are being increasingly reported. Altered mental status was the second most common presentation, comprising encephalopathy or encephalitis and primary psychiatric diagnoses, often occurring in younger patients. The neurological community were alerted to the high prevalence of anosmia and dysgeusia in early reports of COVID-19. Some of these early cohorts also featured non-specific neurological symptoms, such as dizziness and headache. However, severe neurological and neuropsychiatric presentations associated with COVID-19 have become increasingly apparent, including a patient with encephalitis in China in whom SARS-CoV-2 was identified in cerebrospinal fluid (CSF), a patient with acute necrotising encephalopathy in Japan, and cases of cerebrovascular disease (Varatharaj 2020).

CONCLUSION

The opinion is that psychiatric comorbidities in neurological patients, but also physical comorbidities in psychiatric patients are often underestimated or misdiagnosed. In psychiatric patients, this phenomenon can be explained by the fact that these patients visit health facilities less frequently (Newcomwer 2006). In neurological patients, assessment of mental status should become a routine practice, since the presence of a psychiatric disorder can significantly affect the progression and management of the disease. Researchers agree that people with serious mental disorders are more likely to have worse physical health status than people without a mental disorder. Mental and psychiatric disorders that may have an etiological relationship are often declared comorbidities because it is difficult to determine the exact time of their occurrence.

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