

PSYCHIATRIC DISORDERS IN NEUROLOGY

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SUMMARY

Psychiatric disorders (PDs) in neurology are more frequent than it verified in routine exam, not only in the less developed but also in large and very developed neurological departments. Furthermore, psychiatric symptoms (PSs) in neurological disorders (NDs) among primary health care physicians and other specialties are often neglected. Anxiety and depression are most common, but hallucinations, delusions, obsessive-compulsive disorder and delirium or confusional state are also frequent comorbidity in many neurological conditions such as stroke, epilepsy, multiple sclerosis (MS), Parkinson disease (PD). Depression and NDs also have a bidirectional relationship, as not only are patients, for example with stroke at greater risk of developing depression, but patients with depression have a two-fold greater risk of developing a stroke, even after controlling for other risk factors.

Dementia or cognitive impairment are part of clinical picture of PD, stroke patients, patients with MS, Huntington disease etc. The prototype of dementia in PD and other NDs is a dysexecutive syndrome with impaired attention, executive functions and secondarily impaired memory. So-called "functional" (or psychogenic or hysterical/conversion) symptoms are relatively infrequent in "neurological" conditions, but very often unrecognized and not properly treated.

Treatment of PSs in neurology, basically are not different than treatment of these symptoms in psychiatry and should be include pharmacotherapy and psychiatry.

This presentation gives an overview of frequency and type of PSs underlying necessity to recognize these disorders in every day routine exam and properly treatment.

Key words: psychiatric disorders – neurology

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INTRODUCTION

Psychiatric disorders (PDs) in neurology are more frequent than it verified in routine exam, not only in the less developed but also in large and very developed neurological departments (Moriarty 2007, Jefferies et al. 2007). Furthermore, psychiatric symptoms (PSs) in neurological disorders (NDs) among primary health care physicians and other specialties are often neglected. Anxiety and depression are most common, but hallucinations, delusions, obsessive-compulsive disorder and delirium or confusional state are also frequent comorbidity in many neurological conditions such as stroke, epilepsy, multiple sclerosis (MS), Parkinson disease (PD) (Kanner 2005).

Clinical neurologists and psychiatrists have long recognized the frequent occurrence of psychiatric conditions in the context of neurologic (brain) disease. Indeed, this frequent co-occurrence of psychiatric with neurologic symptoms should come as no surprise, since psychiatric disorders, such as schizophrenia and the mood disorders, can be induced by structural brain disease. Presumably, brain dysfunction from conditions that cause neurologic symptoms - such as seizures, and impairments in movement, sensation, speech, or language - also affects areas of the brain that regulate mood, emotion, cognition, and perception (Lyketsos, Kozauer & Rabins 2007).

STROKE

Stroke can be defined a sudden attack of a specific neurological deficit, caused by thrombosis or hemor-

rhage in the cerebral circulation, and it is the third leading cause of death in developed countries (Lyketsos, Kozauer & Rabins 2007, Devasenapathy & Hachinski 2004). Psychiatric syndromes associated with stroke lead to significant psychological distress, functional impairments, poor rehabilitation outcomes, and excess mortality (Lyketsos, Kozauer & Rabins 2007, Morris et al. 1993). The most common psychiatric disturbances seen after stroke include cognitive impairment and dementia, depression, mania, anxiety disorders, and pathological laughing and crying - now referred to as involuntary emotion expression disorder or IEDD (Cummings et al. 2006).

Cognitive deficits of several types have been reported, typically in relationship to the location of brain injury. Left-hemisphere strokes frequently cause dysphasia, whereas righthemisphere strokes are associated with anosognosia, inattention, impaired spatial reasoning, and neglect syndromes. Motivation, memory, judgment, and impulse control may be affected after frontal stroke. Additionally, brain vascular disease is associated with the emergence of dementia. This can be the result of one stroke affecting a single critical area, such as the thalamus, several strokes affecting areas important to cognition, or chronic vascular insufficiency leading to white-matter changes with associated cognitive problems ("vascular cognitive impairment") (Roman et al. 2004, Sinanović 2010, Sinanović et al. 2011).

Depression following a stroke, also referred to as post-stroke depression (PSD), is one of the more frequent complications of stroke, and has significant negative consequences on the recovery of motor and

cognitive deficits, as well as the mortality risks associated with stroke, and has negative consequences on the recovery of motor and cognitive deficits, as well as the mortality risks associated with stroke. The prevalence of PSD has ranged from 5 to 63% of patients in several cross-sectional studies, peaking three to six months after a stroke, peaking three to six months after stroke (Kanner 2005, Sinanović 2010, Robinson 2003). The systematic review of 51 studies (reported in 96 publications) conducted between 1977 and 2002 by Maree et al. (2005) showed that frequencies of depression varied considerably across studies, but the pooled estimate was 33% (95% confidence interval, 29% to 36%) of all stroke survivors experiencing depression.

Major depression and minor depression are the most frequently recognized expression of PSD, and clinical manifestations of PSD are similar to those of idiosyncratic late-onset depression, but psychomotor retardation may be frequently identified. Twenty-five percent of patients hospitalized with an acute stroke develop major depression which is phenomenologically indistinguishable from idiopathic major depression (Lyketsos, Kozauer & Rabins 2007). Moreover, depression in stroke also have a bidirectional relationship, as not only are patients with stroke at greater risk of developing depression, but patients with depression have a two-fold greater risk of developing a stroke, even after controlling for other risk factors (Kanner 2005, Sinanović 2010).

Anxiety accompanies a large number of neurological disorders, has been observed in many medical conditions, and may be induced by a wide variety of substances (Cummings & Mege 2003, Cunnings 1995). Anxiety that is manifestation of the brain disorder resembles the symptomatology of idiopathic generalized anxiety disorder (GAD), including excessive worry or unwarranted apprehension: shakiness, trembling, and restlessness; shortness of breath; palpitations, excessive sweating; clammy hands, dry mouth, light-headedness, flushes or chills, and frequent urination; and agitation, increased startle response, poor concentration, and irritability (Starkstein 1990). In a study by Starkstein et al (1990) GAD was found in 24% of patients with acute stroke. Most of these patients also had a diagnosis of major depression. GAD alone was found in 6%. In a study by Castillo et al (1993) GAD occurred in 11% of nondepressed stroke patients. In one our previous study (Ibrahimagić, Sinanović & Smajlović 2005) anxiety was found in 30% of patients 48 hours after acute stroke and in 25% after 15 days of stroke onset. Accordint to stady made by Astrom (1996) the prevalence of GAD after stroke was 28% in the acute stage, and there was no significant decrease through the 3 years of follow-up. At 1 year, only 23% of the patients with early GAD (0 to 3 months) had recovered; those not recovered at this follow-up had a high risk of a chronic development of the anxiety disorder. Comorbidity with major depression was high and seemed to impair the prognosis of depression. At the acute stage after stroke, GAD plus

depression was associated with left hemispheric lesion, whereas anxiety alone was associated with right hemispheric lesion. Cerebral atrophy was associated with both depression and anxiety disorder late but not early after stroke.

Delirium, synonymous with the acute confusional state, is a condition of relatively abrupt onset and short duration whose major behavioural characteristics are altered attention. It is acute reversible mental disorders characterized by confessional state with disorientation for time or place (Cummings & Mege 2003). Other behavioural abnormalities frequently coexist including mood and emotional alterations, illusions, hallucinations with increased or decreased psychomotor activity. There are different reports on frequency of delirium in acute stroke, from 24 to 48%, and it is more frequent in hemorrhagic then ischemic stoke (Sinanović 2010, Robinson 2003, Sinanović, Vidović & Smajlović 2006). Delirium is not stabile state. The level of consciousness may be reduced or may fluctuate between drowsiness and hypervigilance, but the patient is unable to maintain attention for any substantial period of time. The principal effort in the management of the patient in delirium is directed at identifying and treating the underlying disease process (Sinanović 2010).

PARKINSON'S DISEASE

Nowadays, Parkinson's disease (PD) is generally considered a multifaceted disease with a broad spectrum of symptoms, and has been associated with cognitive disorders, affective disorders, psychotic phenomena, impulse control disorders, and problematic repetitive behaviors (Lyketsos, Kozauer & Rabins 2007). In an era where the motor symptoms can be relatively well controlled with L-dopa in the early and middle stages of PD, the psychiatric syndromes are often a major source of disability, distress, and quality of life impairment for both patients and caregivers. Most patients with PD experience some cognitive impairment, with 25% to 40% developing dementia over the course of their illness. Longitudinal studies suggest that the type and severity of cognitive disturbances is stagedependent. In early stages, patients primarily develop problems with memory and information processing, probably as a result of the disease's primary involvement of subcortical structures. In later stages, impairments in cortical functions, such as dyspraxia and amnesia, emerge in many patients (Kaner 2005, Lyketsos, Kozauer & Rabins 2007, Marsh & Berk 2003).

Depressive disturbances are common in PD, with a prevalence of 25% to 50% over the course of the illness. Fewer than half have major depression; most patients have milder forms of depression referred to as dysthymia or subsyndromal depression (Kanner 2005, Lyketsos, Kozauer & Rabins 2007). In one our previous study (Sinanović, Hudić & Ibrahimagić 2007) some depressive symptoms were present in all 35 PD patients,

but moderate depression in 22.85% and severe in 45.71%. As in the case of epilepsy and stroke, depression and PD appear to have a bidirectional relationship. That is, not only are patients with PD at greater risk to developing depression, but patients with a depressive disorder have been found to be at greater risk of developing PD (Kanner 2005, Nilson, Kissing & Bowling 2001).

Anxiety is very common in PD, but has not been sufficiently studied. Up to 40% of PD patients have anxiety symptoms. Panic disorder is very common, with a prevalence as high as 25%. Panic attacks are fairly typical in their form, in that they are of sudden onset with apprehension and anxiety, associated fears of having a heart attack or dying, and a range of uncomfortable accompanying physical symptoms. The comorbidity of depressive and anxiety disorders in PD is common; most of the time neither occurs alone (Lyketsos, Kozauer & Rabins 2007, Schneider et al. 2008).

According to recent review paper by Leentjens (Leentjens 2012) the prevalence and cumulative incidence of psychopathological symptoms is high. The reported prevalence is 17% for major depressive disorder, 34% for anxiety disorder, 17% for apathy, 14% for impulse control disorders, 88% for sleep disturbances and 60% for sexual problems. The cumulative incidence of hallucinations is 60%. Mild cognitive impairment is present in at least 50% with a cumulative incidence of 66% for dementia after 12 years. All psychopathological syndromes have a strong negative impact on a number of disease parameters, other psychiatric comorbidity, and quality of life. All psychopathological syndromes tend to occur with higher frequency in patients with the hypokinetic rigid type of PD. Other risk factors divide into general and disease-specific risk factors, and may vary between the different syndromes.

EPILEPSY

Up to 50% of patients with epilepsy have psychiatric syndromes. Cognitive, mood, anxiety, and psychotic disturbances are most common (Lyketsos, Kozauer & Rabins 2007, Cummings & Mege 2003). Since the epilepsies are heterogeneous and chronic conditions, this complexity is also reflected in the associated psychiatric disturbances. For the most part, psychiatric disturbances have been categorized according to whether they are direct expressions of a seizure, features of a postictal state, or phenomena that occur during the interictal period. The majority of psychiatric syndromes in epilepsy occur in the interictal period, and thus probably have more to do with the state of the brain in the absence of excessive electrical discharge than with the discharge itself (Lyketsos, Kozauer & Rabins 2007).

Depression is the most common psychiatric comorbidity in patients with epilepsy. Prevalence of is higher than in a matched population of healthy controls,

and ranges from 3.9% in patients with controlled epilepsy to 20-55 in patients with recurrent seizures (Lyketsos, Kozauer & Rabins 2007). As in the case of Parkinson's disease and stroke, depression and epilepsy appear to have also a bidirectional relationship (Kanner 2005, Sinanović 2010).

The clinical presentation of depressive disturbances is for the most part typical for idiopathic depression. However, about a third of patients with epilepsy present with atypical features of depression that tend to be intermittent. They also resemble dysthymia and include anhedonia, fatigue, anxiety, and irritability with less prominent impairments in self-attitude, self-depreciative ideas, or suicidal ideation.

The rate of manic syndromes appear to be higher in epilepsy, and these usually are atypical in presentation and more likely to present with irritability and overactivity than idiopathic bipolar disorder, which itself does not appear to be more prevalent in epilepsy relative to the general population. This has led to the belief that epilepsy-associated brain damage is a major component in the occurrence of mania and temporal lobe epilepsy.

The prevalence of psychotic symptoms in interictal periods is on the order of 5% to 7% in patients with epilepsy. In patients with temporal lobe epilepsy, these disturbances are often schizophrenia-like in their presentation. Paranoid or persecutory delusions and both visual and auditory hallucinations have been reported. Also "negative symptoms" of schizophrenia such as amotivation, apathy, flattened affect, and disorganized behavior have been reported in association with delusions and hallucinations. This has given rise to the hypothesis of the "schizophrenialike psychoses of epilepsy" which remains controversial (Lyketsos, Kozauer & Rabins 2007, Lyketsos et al. 1993).

MULTIPLE SCLEROSIS

Psychiatric syndromes seen in multiple sclerosis (MS) include demoralization, major depression, mania, involuntary emotion expression disorder, cognitive impairment, and psychosis. Demoralization is particularly complex in the context of MS because of the intermittent nature of the condition, which can make it particularly difficult to cope with. Patients usually have more difficulty adapting to acute rather than gradual changes in disease course. They can become increasingly demoralized in a condition that remits, remains quiescent for a while, and then returns, often with more severe symptoms. Several studies suggest that over time many MS patients find it increasingly difficult to adapt psychologically to new episodes and that this can adversely impact their relationships and psychosocial functioning (Lyketsos, Kozauer & Rabins 2007, Mohr et al. 1999).

The high prevalence of depression was recognized in Charcot's early characterization of MS. Review of

various studies has indicated the presence of depressive symptoms in approximately 80% of all patients with MS, and estimated lifetime prevalence rates of major depressive disorders to range from 10-60% (Kanner 2005, Minden & Schiffer 1990).

Diagnosing depression in an MS patient can be difficult because many symptoms such as sleep disorder, fatigue, and apathy overlap with the primary disease. Nevertheless, with careful clinical assessment, depression can be confidently diagnosed. It is a major source of disability and quality of life impairment. Suicidal ideation is fairly prominent in MS patients with the prevalence across the disease of the order of 30 % (Feinstein 2002). Treatment of depression in MS should include pharmacotherapy and different types of psychotherapy. There are a few controlled studies that have examined the pharmacotherapy responses of depression in MS patients, and treatment basically should be the same as treatment of idiopathic depression (Kanner 2005).

Euphoria and other manic symptoms have been reported in MS patients back to the days of Charcot. Up to 10% of patients develop euphoria or more severe forms of mania. Additionally, euphoria and mania can be the result of MS treatments, and in particular steroid use.

Cognitive impairment occurs in 40-65% of multiple sclerosis (MS) patients, typically involving complex attention, information processing speed, (episodic) memory and executive functions. It is seen in the subclinical radiologically isolated syndrome, clinically isolated syndrome, and all phases of clinical MS. In pediatric-onset MS cognition is frequently impaired and worsens relatively rapidly. Cognitive impairment often affects personal life and vocational status. Depression, anxiety and fatigue aggravate symptoms, whereas cognitive reserve partially protects. Cognitive dysfunction correlates to brain magnetic resonance imaging (MRI) lesion volumes and (regional) atrophy, and degree of and increase in MRI abnormalities predict further worsening (Jongen, Ter Horst & Brands 2012).

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REFERENCES

1. Astrom M. Generalized anxiety disorder in stroke patients - a 3-year longitudinal study. *Stroke* 1996; 27: 270-275.
2. Castillo S, Starkstein SE, Fedoroff P, Price TR, Robinson RG. Generalized anxiety after stroke. *J Nerv Ment Dis* 1993; 181:100-106.
3. Cummings JL, Mege MS. *Neuropsychiatry and Behavioral Neuroscience*. Oxford: Oxford University Press, 2003.
4. Cummings JL, Arciniegas DB, Brooks BR, et al. Defining and diagnosing involuntary emotional expression disorder. *CNS Spectr* 2006; 11:1-7.
5. Cunnings J. *Neuropsychiatry*. In: Simpson MG (ed). New York: Impact Communications, Inc, 1995; 109-136.
6. Devasenapathy A, Hachinski V. *Cerebrovascular Disease*. In: Rizzo M, Eslinger JP (eds). *Behavioral Neurology and Neuropsychology*. Philadelphia: W.B. Saunders Company, 2004; 597-613.
7. Feinstein A. An examination of suicidal intent in patients with multiple sclerosis. *Neurology* 2002; 59: 674-678.
8. Ibrahimagić OČ, Sinanović O, Smajlović D. Anxiety in acute phase of ischemic stroke and myocardial infarction. *Med Arh* 2005; 59:366-369.
9. Jefferies K, Owino A, Rickards H, Agrawal N. Psychiatric disorders in inpatients on a neurology ward: estimate of prevalence and usefulness of screening questionnaires. *Neurol Neurosurg Psychiatry* 2007; 78:414-416.
10. Jongen PJ, Ter Horst AT, Brands AM. Cognitive impairment in multiple sclerosis. *Minerva Med* 2012; 103:73-96.
11. Kanner MK. *Depression in Neurological Disorders*. Wilingham: Cambridge Medical Communication Ltd, 2005.
12. Leentjens AFG. Epidemiology of psychiatric symptoms in Parkinson's disease. *Adv Biol Psychiatry* 2012; 27:1-12.
13. Lyketsos CG, Stoline AM, Longstreet P, Lesser R, Fisher R, Folstein MF. Mania in temporal lobe epilepsy. *Neuropsychiat Neuropsychol Behav Neurol* 1993; 6:19-25.
14. Lyketsos GC, Kozauer N, Rabins VP. Psychiatric manifestations of neurological disease: where are we headed? *Dialogues Clin Neurosci* 2007; 9:111-124.
15. Maree LH, Yapa C, Parag V, Anderson CS. Frequency of depression after stroke. A systematic review of observational studies. *Stroke* 2005; 36:1330-1343.
16. Marsh L, Berk A. Neuropsychiatric aspects of Parkinson's disease. *Recent advances Curr Psychiatry Rep* 2003; 5:68-76.
17. Minden SL, Schiffer RB. Affective disorders in multiple sclerosis, review and recommendations for clinical research. *Arch Neurol* 1990; 47:98-104.
18. Mohr DC, Dick LP, Russo D et al. The psychosocial impact of multiple sclerosis: exploring the patient's perspective. *Health Psychol* 1999; 18:376-382.
19. Moriarty J. Psychiatric disorders in neurology. *J Neurol Neurosurg Psychiatry* 2007; 78: 331.
20. Morris PL, Robinson RG, Andrezjewski P, Samuels J, Price TR. Association of depression with 10-year post-stroke mortality. *Am J Psychiatry* 1993; 150:124-129.
21. Nilson FM, Kissing LV, Bowling TG. Increased risk of developing Parkinson's disease for patients with major affective disorder a register study. *Acta Psychiatr Scand* 2001; 104:380-386.
22. Robinson RG. Poststroke depression. Prevalence, diagnosis, treatment and disease progression. *Biol Psychiatry* 2003; 54:376-387.
23. Roman GC, Sachdev P, Royall DR et al. Vascular cognitive disorder: a new diagnostic category updating vascular cognitive impairment and vascular dementia. *J Neurol Sci* 2004; 226:81-87.
24. Schneider F, Althaus A, Backes V, Dodel R. Psychiatric symptoms in Parkinson's disease. *Eur Arch Psychiatry Clin Neurosci* 2008; 258 (Suppl 5): 55-59.
25. Siegert RJ, Abernethy DA. Depression in multiple sclerosis: a review. *J Neurol Neurosurg Psychiatry* 2005; 76:469-475.

26. Sinanović O, Vidović M, Smajlović Dž. Najčešći neuropsihološki poremećaji u akutnom cerebrovaskularnom inzultu. *Liječ Vjesn* 2006; 128 (Supl 6): 20-21.
27. Sinanović O, Hudić J, Ibrahimagić O. Dementia and depression in Parkinson's disease. *Parkinsonism Relat Disord* 2007; 13 (Suppl 2): S53
28. Sinanović O. Neuropsychology of acute stroke. *Psychiat Danub* 2010; 22:278-281.
29. Sinanović O, Mrkonjić Z, Zukić S, Vidović M, Imamović K. Post-stroke language disorders. *Acta Clin Croat* 2011; 50:77-92.
30. Starkstein SE, Cohen BS, Fedoroff P, Parikh RM, Price TR, Robinson RG. Relationship between anxiety disorders and depressive disorders in patients with cerebrovascular injury. *Arch Gen Psychiatry* 1990; 47:246-251.

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