sciendo

ARS Medica Tomitana - 2023; 1(29): pag. 36 - 45
doi: 10.2478/arsm-2023-0007

UNVEILING THE MIND: A COMPREHENSIVE REVIEW OF PSYCHIATRIC DISORDERS IN PARKINSON'S DISEASE

Alina Zorina Stuparu[1,2], Eda Ciorabai[1,3], Camelia Pantu[3], Alexandru Floris Stuparu[4], Lavinia Muja[1,2], Diana Vranau[2], Silviu Docu Axelerad[5], Any Axelerad[1,2]

[1] Faculty of Medicine, University "Ovidius" of Constanta
[2] Department of Neurology, "Sf Apostol Andrei" County Hospital of Constanta
[3] Department of Psychiatry, "Sf Apostol Andrei" County Hospital of Constanta
[4] Department of Orthopedy and Traumatology, "Sf Apostol Andrei" County Hospital of Constanta
[5] "Brainaxy" Clinic Constanta

Alina Zorina Stuparu

email: zorina.stroe@yahoo.com

ABSTRACT

Background/Aim: The primary objective of this research was to evaluate the findings and conclusions presented in existing literature articles pertaining to mental illnesses in patients with Parkinson's disease. Patients and Methods: The study used a patients and methods approach. The study also comprised studies and papers that provided information on clinical aspects, as well as links and correlations between Parkinson's disease and mental illnesses. Results: Symptoms of mental disorders are extremely prevalent in PD, but they are frequently undetected, undertreated, and overlooked if not evaluated precisely. Neuropsychiatric disorders of Parkinson's disease divide into a number of major groups: anxiety and mood disorders, psychosis, behavioral modifications such as sexual disorders, impulse control disorders, dopaminergic medication abuse, and sleeping disorders. Conclusion: The majority of mental health conditions in PD are treatable, and failure to do so has a negative impact. Numerous investigations demonstrate that psychiatric symptoms influence the quality of life more than motor manifestations. Depression seems to be associated with deterioration in cognitive performance, tasks associated with everyday living, and motor performance and might have the greatest influence on the quality of life in PD. Psychosis is the leading cause of caretaker concern and a significant predictor of nursing residence relocation. The objective of therapy for mental illnesses in PD ought to include remission; inadequate treatment must be avoided.

Keywords: psychiatric disorders, Parkinson's disease, anxiety, depression, apathy.

Introduction

Parkinson's disease (PD) is the prototypical neuropsychiatric condition (1). Despite the fact that PD is characterized through its motor disorders, mental and behavioral abnormalities play a significant role. They occur in nearly every patient and frequently they affect the patient more in comparison to motor dysfunctions. Due to the confluence between motor, cognitive, and psychiatric traits, it may be challenging to differentiate primary motor aspects of PD on a mental health assessment from psychiatric disorder features.

For instance, limited affective responsiveness may indicate the motor sign of facial masking, the diminished influence of a clinical depression, abulia emerging from frontal-subcortical dysfunction, or inattentiveness and confusion caused by anticholinergic treatments. Such an equivocation leads to the underdiagnosis or undertreatment of psychiatric conditions (2). The successful treatment of Parkinson's disease entails intentional and continuous surveillance and therapy for neuropsychiatric disorders.

Numerous variables lead to neuropsychiatric symptoms in Parkinson's disease. Concerns of PD could induce hopelessness, anxiety, and depression. Nevertheless, the majority of disturbances tend to be closely correlated to the

neurobiology of PD or its management (3). In parallel to nigrostriatal dopaminergic decline, PD impacts mental and emotional processes-related frontal and limbic dopamine systems.

Deterioration of serotonergic, noradrenergic, and cholinergic neurons contributes to intellectual and psychiatric dysfunction. Numerous different abnormalities, including such emotional lability correlated to ‚on–off' motor fluctuations, are linked with PD therapy (4). Psychiatric conditions can be induced by dopaminergic and other antiparkinsonian medications or neurosurgical interventions. For instance, anticholinergic drugs frequently affect cognitive function or induce psychosis or delirium.

A significant volume of research explains the cognitive and behavioral side effects of deep brain stimulation, especially when treating simultaneous both subthalamic nuclei (5). These involve the deterioration or appearance of verbal, memory, and emotional impairments, as well as a rise in the likelihood of suicide (6).

PD consequences, including unsteadiness, can precipitate a succession of psychiatric issues. It can vary from fear of falling to delirium with nervous conduct because of a subdural hematoma caused by a fall. Depression and anxiety conditions are also frequently present prior to the diagnosis of PD. As a result, affective conditions may be possible causes of or precursors to Parkinson's disease (7).

The effects of neuropsychiatric disorders in Parkinson's disease expand further than the manifestations. They have a greater impact on quality of life and functional impairment compared to motor deficits, dyskinesias, and motor fluctuations (8). Depression has the most detrimental influence on life quality. It is also linked to greater and worsening motor and mental impairments, reduced daily living activities, additional mental health and medical conditions, caregiver perceived stress, and depression (9).

Method

The present study used a compilation of scholarly resources, including research papers, reviews, and original articles, obtained via the utilization of the 'PubMed' search engine. The inclusion criteria used for the articles were as follows: This study encompasses research published through August 1, 2023, English language. The inclusion criteria for patients are as follows: age 18 years or older, a diagnosis of Parkinson's disease, and the inclusion of correlations and relationships between Parkinson's disease and mental illnesses in the study design.

Results and discussion

Clinical psychiatric condition features in PD

Cognitive abnormalities

The cognitive decline associated with PD, which extends from modest selective abnormalities to global dementia, can sometimes not be apparent (10). Also for those who have dementia, scores on dementia diagnostic tests, such as the Mini-Mental State Examination, are frequently within the healthy range. Sooner on in Parkinson's disease, executive and visuospatial processes, memory, and attention are affected by specific deficits. Furthermore impacted are data processing as well as verbal fluency. Memory impairment impact explicit recall more than recognition memory, and there is no ‚fast forgetting' or aphasia, as is typical of Alzheimer's disease (AD).

These impairments manifest as problems with disorganization, planning, establishing priorities, neglect, and attention deficits, and they can have a negative impact on employment and independent living.

Dementia typically manifests later in life, is characterized by global abnormalities that prevent functional independence, and generally occurs into three groups (11).

In the initial instance, selective deficits are exacerbated, especially in memory and information processing. A second category demonstrates a more extensive involvement of brain processes, such as aphasia, apraxia, and memory, but a different clinical trajectory from AD (12). The third category has characteristics of both PD and AD, as well as severe language difficulties. Cross-sectionally, dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PD dementia) have numerous similarities. In

DLB, symptoms of dementia whether anticipate the development of parkinsonism or appear shortly after the occurrence of motor symptoms. Additionally, DLB is characterised by visual vivid hallucinations and changing attentional states. Parkinsonism in DLB could respond to levodopa treatment, but adverse effects, especially psychosis, could be increased (13).

Delirium should always be investigated, a frequent condition of global cognitive decline in Parkinson's disease. Psychoactive medications utilised alleviate Parkinson's disease or psychiatric conditions (e.g., anticholinergics, dopamine agonists, benzodiazepines, hypnotics, and pain medications) are common causes of delirium (14). Frequently, delirium associates both dementia and moderate cognitive decline, resulting in a worsening of cognitive decline related to baseline. Confusion and disorientation are the predominant characteristics. Mental condition oscillations, including lucidity in the morning and disorientation and agitation in the evening, could be obscured by on–off motor fluctuations, particularly in advanced Parkinson's disease and dementia.

Affective conditions

In addition to prolonged changes in mood, affective disorders exhibit significant somatic symptoms, impaired judgment, and vegetative symptoms (sleep and appetite disturbances) that correspond to characteristics of PD. Consequently, direct inquest in to the mood patterns is essential for detecting affective disorders. If not, these diagnoses will be ignored (15). The patient's older age or the struggles of PD could result in a determination that affective disturbances seem to be „understandable." Comparable to certain other health conditions, affective disorders consist of a collection of symptoms and signs with an usually expected trajectory and outcome, as opposed to emotional responses to particular concerns or situations (16).

Depression, apathy, and pseudobulbar affect

Depression is more prevalent in PD compared to other chronic conditions; the intensity of symptoms of depression in PD is unrelated to the length of motor ailments or the severity of motor manifestations. Additionally, "sub-syndromal" depression generates considerable distress and disability (17). Depression contributes to the worsening of cognitive impairments in PD and frequently co-occurs alongside other psychiatric disorders (18).

Previous research indicates that depression in PD can be defined by additional dysphoria and irritation, as well as less remorse and suicidal thoughts compared to idiopathic depression. However, particular instances demonstrate the spectrum of depressive manifestations. Bradykinesia, or slowed motor movements and decreased facial expression are noticeable characteristics of PD that have similarities to psychomotor slowing, that, together with PD manifestations such as tiredness and sleep difficulties, are common with Diagnostic and Statistical Manual (DSM)-IV-TR guidelines for major depressive disorder (MDD) (18). Concentrating on affective symptoms as opposed to neuro vegetative complaints can facilitate the diagnosis of depression in PD. A method to differentiate depressive syndromes from PD symptoms is to question patients about their passions and observe whether they light up, participate in dialogue, or talk about current activities which offer them joy (19).

Major depression, minor depression, and dysthymia are more prevalent in PD compared to other chronic diseases. There are not any clear correlations between the onset age, duration, severity of PD or PD stage or subtype, the timeline of depression commencement, or the severity of depression in patients with PD (20). Depression in patients with moderate PD could be significantly more debilitating and problematic than the motor impairment. When self-reported impairment surpasses what is anticipated from of the evaluation, a diagnosis of depressive disorder must be explored (21). Patients or doctors can be hesitant about accepting a depressive diagnostic because of worries about it's own consequences; but nevertheless, unrecognized and unmanaged psychiatric problems are essentially more challenging.

Focusing on emotional changes as opposed to neurovegetative symptoms facilitates diagnosis (22). Comparable to major depression in patients without neurological disease, the basic components of major depressive disorder are a chronic and ubiquitous negative mood,

a decreased ability to appreciate otherwise pleasurable activities (anhedonia), or a decrease in one's normal baseline interest in activities (20). Due to motor symptoms, non - depressed PD patients could restrict their activities, whereas depressed PD patients will not search alternative activities to appreciate. Nonsomatic depressive characteristics, such as extreme pessimism, negative ruminations, emotional instability, helplessness, and remorse, differentiate depressed PD patients from those without depression. Several research suggests that self-blame, a negative self-attitude, delusions, and suicidal behavior are much less prevalent in PD patients with significant depression (21, 22). Nonetheless, these behaviors may persist. Non-major depressive disorders exhibit similar patterns, although with attenuated and reduced manifestations. Perhaps ‚subsyndromal' depressive disorders lead to substantial distress.

Having problems coping is a crucial indicator. In the confronting of recurrent mood disorders, efficient managing and adaptation are extremely difficult. People adapt and confront difficulties associated with PD after treatment, indicating that the mood disorder is improving with therapy – many patients report, „I can manage with PD, but not when despondent." Therapists could perhaps inquire explicitly about emotions such as despair and hopelessness, as well as suicidal and homicidal impulses (20-22).

Apathy

Apathy, a condition characterized by decreased motivation and lowered self-initiated target affective, cognitive, and behavioral activity, can manifest as a component of depressive disorders or as an independent entity. Despite the fact that apathy typically does not respond to medications or surgery (i.e., deep-brain stimulation), apathy could appear when dopaminergic treatments are decreased following subthalamic nucleus stimulation. This could be due to a dopaminergic withdrawal syndrome (23). People with this condition display little goal-directed interest in their environment or in themselves and participate in few actions, such as casual discussion. Although apathetic patients rarely complain, their conduct disturbs their caregivers, who might mistakenly interpret it as intentional. Apathy degrades clinical outcomes because apathetic individuals become less inclined to take part in self-care, adhere to therapy, or engage in physical activity (24).

Apathy is additionally prevalent, probably due to depleted dopamine levels (25). Apathetic patients seem disinterested in the world around them, are unconcerned about both themselves and their peers, and participate in very few actions, such as unplanned discussions. Apathy may be a symptom of MDD or an independent condition (24). Apathy also has to be differentiated from the masked face from PD. Decreased testosterone levels can aggravate the apathy associated with Parkinson's disease.

Apathy diminishes positive results in PD, as individuals are not as inclined to engage in taking care of themselves, adhere to therapy, and engage in physical activity. Apathy is frequently overlooked. Individuals who are apathetic don't voice their discontent, but their conduct frequently upsets the people around them. To prevent misinterpreting an individual's conduct as intentional, caretakers must be informed regarding apathy. Individuals with apathy thrive in an organized, enhanced atmosphere because they seldom demonstrate entrepreneurship (26).

Pseudobulbar affect

Pseudobulbar affect, which is additionally known as emotional difficulty or abnormal giggling and weeping is a symptom of Parkinson's disease along with various neurological disorders. Patients with pseudobulbar affect exhibit exaggerated or impulsive emotional responses in a lack of an appropriate emotional situation. Therefore, the pseudobulbar affect indicates a behavioral deviation which may be indicative of a disruption in neural networks as opposed to a mood disorder. Even though the recurrent episodes of crying of pseudobulbar affect typically resemble depression, weeping incidents in pseudobulbar affect are perceived as extreme by individuals who do not experience concomitant sorrow (27).

Pseudobulbar impact, as well characterized as compulsive laughter and weeping or ‚emotional incontinence,' is characterized by excessive, involuntary emotional outbursts that are typically improper and brief, characterized by excessive weeping or laughter in the absence of emotions of sorrow or merriment. In PD, pathological crying

is more prevalent (28). The complaints may result in distress, embarrassment, and psychosocial problems. Frequently, the elevated affectivity happens regardless of a predominant mood disorder. In these kind of situations, nevertheless, patients could mistakenly believe they have a depressive disorder because they weep so frequently in reaction to sorrowful or frightening stimuli (29). Additionally, benzodiazepines and delirium are linked to pseudobulbar impact. When pseudo-bulbar impact is predominant, especially at the commencement of the motor impairment, both parkinsonian conditions including progressive supranuclear palsy must be investigated.

Mania

Mania and hypomania in Parkinson's disease usually originate from dopaminergic or additional PD therapies, rather than from the disease itself. Nevertheless, certain individuals experience bipolar disorder prior to the advent of Parkinson's disease and eventually develop PD (30).

The underlying cause of mania due to medications or another medical condition must be treated. Mania caused by dopaminergic therapy can be treated by adjusting dopaminergic medicine. If no particular cause of mania is able to determine, medications that stabilize mood could be taken into account, yet their efficacy in PD is still being investigated.

In PD, mania and hypomania are insufficiently described. A few individuals may present with bipolar disorder, a chronic affective disorder manifested by depressive and hypomanic or manic episodes, prior to the onset of Parkinson's disease. Nevertheless, isolated manic events are most frequently caused by dopaminergic therapy or neurosurgical procedures. In the ‚on' state, a few patients exhibit hypomanic characteristics, including enhanced irritability. Mania and hypomania manifest comparably to non-PD patients, with the exception of mood fluctuations in certain individuals (31). Symptoms involve elevated mood and self-worth, irritability, restlessness, and enhanced goal-directed activity, as well as hazardous behaviors and emotional psychotic manifestations.

Anxiety

Despite patients with PD can suffer from reactionary anxiety due to illness-related issues, the majority of anxiety disorders in PD are unrelated to motor severity (32). Actually, they indicate to be involved with the fundamental neurological modifications involved with the condition, which frequently manifest prodromal prior to PD being identified. The most prevalent anxiety-related conditions in PD are panic disorder, a form of generalized anxiety disorder, and social phobia, but several anxiety diseases in PD cannot be categorized into traditional DSM classifications (33).

OCD is not more common in people with Parkinson's disease compared to the general population. Individuals with Parkinson's disease, particularly those with severe symptoms, may show repetitive, stereotypical behaviors that have similarities to OCD but do not have real obsessive or compulsive defining features (34). Anxiety disorders and depression are frequently associated with PD. The coexistence of the physical manifestations of anxiety and PD – tremors, sleep impairments, diminished focused attention, and diaphoresis – complicates diagnosis (35). Concentrating on the affective manifestations of anxiety disorders can help with their identification.

Anxiety interventions for Parkinson's disease have not been rigorously investigated; therefore, present methods adhere to the broad guidelines used for idiopathic anxiety in older people. Important initial measures include optimizing PD treatment as well as managing associated medical and mental health issues. Due to their beneficial adverse effect characteristics, SSRIs are excellent first-line options (36). Beginning therapy with SSRIs with modest concentrations and gradually increasing them could decrease the risk of acute anxiety increases. Benzodiazepines can decrease anxiety but raise the currently elevated risk of disorientation and injuries among individuals with Parkinson's disease; they must be limited to instances in which different treatments did not succeed. Psychotherapy, specifically cognitive-behavioral therapy, could be advantageous (37).

Psychotic conditions

In PD, psychotic symptoms involve hallucinations and delusions (2). Psychosis and concomitant dopaminergic treatments are linked. Remarkably, psychosis in Parkinson's disease is not specifically associated with dopaminergic medications (38). Cognitive impairment, notably dementia, and lack of sleep are caused by significant risk factors. Although psychotic symptoms associated with Parkinson's disease usually develop without any signs of delirium, the probability of delirium must always be evaluated whenever a patient experiences novel or exacerbating psychotic symptoms.

With the exception of the final stages of the disease, psychotic symptomatology in PD is usually linked to one or more drugs used in PD. Whenever psychosis appears prior to dopaminergic therapy, a diagnosis of DLB should be considered. Altered vision, advanced PD, and mental, mood, and sleeping issues are risk factors for psychotic symptomatology in PD. Indicators of psychosis may develop separately from other psychiatric features or they might be a component of a mood disorder, dementia, or delirium (35).

Delusions generally appear in individuals who have previous episodes of hallucinations, whereas the topic of each could be unconnected. Frequent delusional topics contain paranoid thoughts, including opinions regarding marital misconduct, conspiracy theories or concerns of being poisoned. Peculiar delusions as well appear. Persecutory psychotic elements can consequence in hazardous conducts (38).

Discussions

Despite being classified as a movement disorder, PD involves motor, cognitive, and psychiatric symptoms that can be challenging to differentiate. When a patient with PD exhibits minimal emotional reactivity, this is indicative of the attenuated effect of depression, the abulia associated with frontal-subcortical dysfunction, or the motor sign of facial masking. The prevalence of psychiatric concurrent medical conditions in PD and such enigmatic occurrences frequently necesitate psychiatric evaluation.

Verifying that an individual with PD and psychiatric symptoms genuinely has PD is the initial approach in managing the individual. PD can be distinguished from other varieties of parkinsonism by its distinctive symptomatology (39). In Parkinson's disease, symptoms or indicators appear unilaterally, develop asymmetrically, and ameliorate with levodopa therapy. In the lack of dopaminergic therapy, early dementia (i.e., throughout one year after the motor symptom start) or early psychosis in the development of the disease increases concern for DLB (40). Though antipsychotics are recognized contributors to parkinsonism, non-psychiatric medicines, including antiemetics, additionally trigger drug-induced parkinsonism that can be misdiagnosed as new-onset PD in elderly patients. Additional causes of gait modifications in older people which may be misconstrued for PD are normal-pressure hydrocephalus and degenerative spinal modifications (40).

Decision-making and treatment in clinical practice

Several supported evidence guidelines for therapy in psychiatric disorders in PD have been developed. The guidelines adhere to the fundamental concepts for treating idiopathic psychiatric disorders in elderly or physically suffering individuals, with an emphasis on minimizing the adverse effects of treatment that could exacerbate PD symptomatology. As inadequate therapy can exacerbate psychiatric symptomatology, it is important to maximize the medical therapy for PD. Psychotherapy is a proven therapy for numerous psychiatric disorders, and it has no adverse effects or exacerbates symptoms of motor dysfunction. Instructing individuals, caregivers, and practitioners regarding the psychiatric characteristics of PD lowers incorrect interpretations of how patients act and can decrease unnecessary conflict between individuals.

Medications utilized for the treatment of Parkinson's disease, specifically dopaminergic and anticholinergic compounds, can cause alterations in mental status. Medical treatments must be evaluated and adjusted as necessary to minimize psychiatric side effects, with attention to the temporal context of when psychiatric signs and symptoms became apparent in relation to PD treatment modifications (40).

Both fatigue and pain are frequent in PD and are frequently interpreted incorrectly for somatization or depressive symptoms. Depression exacerbates pain as well as tiredness, whereas dyskinesias, dystonia, musculoskeletal limitations, and the "off" state can induce excessive pain and tiredness specifically in a lack of psychopathology.

Laboratory and medical imaging results are typically normal in PD, regardless of the presence or absence of mental health symptoms. Modifications could suggest the presence of a non-PD condition causing psychiatric symptoms. Neuropsychological evaluations may determine if cognitive impairments are associated with Parkinson's disease or indicate a different condition, as well as the efficacy of cognitive-enhancing therapies. Neuropsychological assessments and occupational therapy evaluations elucidate the degree of mental capacity as well as recognize compensatory strategies that maximize regions of maintained mental ability.

Conclusion

Psychiatric illnesses are caused by a variety of factors in PD. Several psychiatric symptoms tend to be directly connected to the neurobiology of Parkinson's disease (PD) or its medical management for numerous patients. PD affects frontal-subcortical pathways and modifies neurotransmitters implicated in psychiatric symptoms, including dopamine, norepinephrine, and serotonin. Dopaminergic therapy may lead to psychiatric adverse effects, and anticholinergics may affect cognitive function.

Psychiatric issues are triggered by complications of PD, including a subdural hematoma and cognitive impairment caused by a PD-related accident. Depression and anxiety could be risk factors for Parkinson's disease, because people with PD exhibit higher levels of premorbid depression and anxiety. Along with contributing to motor changes, the „on-off" pattern caused by variations in the dopaminergic activity has been linked with emotional instability. These patients usually encounter euphoria or euthymia during the „on" stage and melancholy or anxiety during the „off" stage. Stress or emotional deterioration may begin before the motor deterioration, indicating that emotional shifts are not caused by the strain of motor variations.

Clinicians must examine all PD patients for either psychiatric disorders, as patients might not voluntarily report symptoms of mental disorders. While patients are not as inclined to supply a complete medical record due to cognitive impairment or impulse control problems, more details coming from relatives or acquaintances may help explain signs and symptoms. As with every individual with psychiatric complaints, individuals with PD must be evaluated for possible self- or other -endangerment.

Conflicts of Interest

The Authors have no conflicts to disclose in relation to this study.

References

1. Aarsland, D.; Kramberger, M.G. Neuropsychiatric Symptoms in Parkinson's Disease. J. Parkinsons. Dis. 2015, 5, 659–667, doi:10.3233/JPD-150604.
2. Shulman, L.M.; Taback, R.L.; Rabinstein, A.A.; Weiner, W.J. Non-Recognition of Depression and Other Non-Motor Symptoms in Parkinson's Disease. Parkinsonism Relat. Disord. 2002, 8, 193–197, doi:10.1016/s1353-8020(01)00015-3.
3. Chaudhuri, K.R.; Healy, D.G.; Schapira, A.H.V.; National Institute for Clinical Excellence Non-Motor Symptoms of Parkinson's Disease: Diagnosis and Management. Lancet Neurol. 2006, 5, 235–245, doi:10.1016/S1474-4422(06)70373-8.
4. Pontone, G.M.; Williams, J.R.; Anderson, K.E.; Chase, G.; Goldstein, S.A.; Grill, S.; Hirsch, E.S.; Lehmann, S.; Little, J.T.; Margolis, R.L.; et al. Prevalence of Anxiety Disorders and Anxiety Subtypes in Patients with Parkinson's Disease: Prevalence of Anxiety Disorders in Patients With PD. Mov. Disord. 2009, 24, 1333–1338, doi:10.1002/mds.22611.
5. Strutt, A.M.; Simpson, R.; Jankovic, J.; York, M.K. Changes in Cognitive-Emotional and Physiological Symptoms of Depression

Following STN-DBS for the Treatment of Parkinson's Disease: Depression Post-STN-DBS. Eur. J. Neurol. 2012, 19, 121–127, doi:10.1111/j.1468-1331.2011.03447.x.
6. Voon, V.; Krack, P.; Lang, A.E.; Lozano, A.M.; Dujardin, K.; Schüpbach, M.; D'Ambrosia, J.; Thobois, S.; Tamma, F.; Herzog, J.; et al. A Multicentre Study on Suicide Outcomes Following Subthalamic Stimulation for Parkinson's Disease. Brain 2008, 131, 2720–2728, doi:10.1093/brain/awn214.
7. Ishihara, L.; Brayne, C. A Systematic Review of Depression and Mental Illness Preceding Parkinson's Disease. Acta Neurol. Scand. 2006, 113, 211–220, doi:10.1111/j.1600-0404.2006.00579.x.
8. Hely, M.A.; Reid, W.G.J.; Adena, M.A.; Halliday, G.M.; Morris, J.G.L. The Sydney Multicenter Study of Parkinson's Disease: The Inevitability of Dementia at 20 Years: Twenty Year Sydney Parkinson's Study. Mov. Disord. 2008, 23, 837–844, doi:10.1002/mds.21956.
9. Marsh, L.; McDonald, W.M.; Cummings, J.; Ravina, B.; NINDS/NIMH Work Group on Depression and Parkinson's Disease Provisional Diagnostic Criteria for Depression in Parkinson's Disease: Report of an NINDS/NIMH Work Group. Mov. Disord. 2006, 21, 148–158, doi:10.1002/mds.20723.
10. Santos-García, D.; de Deus Fonticoba, T.; Cores Bartolomé, C.; Feal Painceiras, M.J.; Paz González, J.M.; Martínez Miró, C.; Jesús, S.; Aguilar, M.; Pastor, P.; Planellas, L.; et al. Risk of Cognitive Impairment in Patients with Parkinson's Disease with Visual Hallucinations and Subjective Cognitive Complaints. J. Clin. Neurol. 2023, 19, 344–357, doi:10.3988/jcn.2022.0186.
11. Dubois, B.; Burn, D.; Goetz, C.; Aarsland, D.; Brown, R.G.; Broe, G.A.; Dickson, D.; Duyckaerts, C.; Cummings, J.; Gauthier, S.; et al. Diagnostic Procedures for Parkinson's Disease Dementia: Recommendations from the Movement Disorder Society Task Force. Mov. Disord. 2007, 22, 2314–2324, doi:10.1002/mds.21844.
12. Kassubek, J. Diagnostic Procedures during the Course of Parkinson's Disease. Basal Ganglia 2014, 4, 15–18, doi:10.1016/j.baga.2014.02.001.
13. Willis, A.W.; Thibault, D.P.; Schmidt, P.N.; Dorsey, E.R.; Weintraub, D. Hospital Care for Mental Health and Substance Abuse Conditions in Parkinson's Disease: Acute Psychiatric Care Of Parkinson Disease. Mov. Disord. 2016, 31, 1810–1819, doi:10.1002/mds.26832.
14. Halje, P.; Brys, I.; Mariman, J.J.; da Cunha, C.; Fuentes, R.; Petersson, P. Oscillations in Cortico-Basal Ganglia Circuits: Implications for Parkinson's Disease and Other Neurologic and Psychiatric Conditions. J. Neurophysiol. 2019, 122, 203–231, doi:10.1152/jn.00590.2018.
15. Sklerov, M.; Browner, N.; Dayan, E.; Rubinow, D.; Frohlich, F. Autonomic and Depression Symptoms in Parkinson's Disease: Clinical Evidence for Overlapping Physiology. J. Parkinsons. Dis. 2022, 12, 1059–1067, doi:10.3233/JPD-213075.
16. Agüera-Ortiz, L.; García-Ramos, R.; Grandas Pérez, F.J.; López-Álvarez, J.; Montes Rodríguez, J.M.; Olazarán Rodríguez, F.J.; Olivera Pueyo, J.; Pelegrín Valero, C.; Porta-Etessam, J. Focus on Depression in Parkinson's Disease: A Delphi Consensus of Experts in Psychiatry, Neurology, and Geriatrics. Parkinsons Dis. 2021, 2021, 6621991, doi:10.1155/2021/6621991.
17. Gallagher, D.A.; Schrag, A. Psychosis, Apathy, Depression and Anxiety in Parkinson's Disease. Neurobiol. Dis. 2012, 46, 581–589, doi:10.1016/j.nbd.2011.12.041.
18. Toloraia, K.; Meyer, A.; Beltrani, S.; Fuhr, P.; Lieb, R.; Gschwandtner, U. Anxiety, Depression, and Apathy as Predictors of Cognitive Decline in Patients with Parkinson's Disease-A Three-Year Follow-up Study. Front. Neurol. 2022, 13, 792830, doi:10.3389/fneur.2022.792830.
19. Luo, R.; Qi, Y.; He, J.; Zheng, X.; Ren, W.; Chang, Y. Analysis of Influencing Factors of Apathy in Patients with Parkinson's Disease. Brain Sci. 2022, 12, 1343, doi:10.3390/brainsci12101343.
20. Starkstein, S.; Dragovic, M.; Jorge, R.; Brockman, S.; Merello, M.; Robinson, R.G.;

Bruce, D.; Wilson, M. Diagnostic Criteria for Depression in Parkinson's Disease: A Study of Symptom Patterns Using Latent Class Analysis: Diagnostic Criteria for Depression in PD. Mov. Disord. 2011, 26, 2239–2245, doi:10.1002/mds.23836.
21. Fontoura, J.L.; Baptista, C.; Pedroso, F. de B.; Pochapski, J.A.; Miyoshi, E.; Ferro, M.M. Depression in Parkinson's Disease: The Contribution from Animal Studies. Parkinsons Dis. 2017, 2017, 1–8, doi:10.1155/2017/9124160.
22. Johnson, A.R.; Lawrence, B.J.; Corti, E.J.; Booth, L.; Gasson, N.; Thomas, M.G.; Loftus, A.M.; Bucks, R.S. Suitability of the Depression, Anxiety, and Stress Scale in Parkinson's Disease. J. Parkinsons. Dis. 2016, 6, 609–616, doi:10.3233/JPD-160842.
23. Starkstein, S.E.; Brockman, S.; Hayhow, B.D. Psychiatric Syndromes in Parkinson's Disease. Curr. Opin. Psychiatry 2012, 25, 468–472, doi:10.1097/YCO.0b013e3283577ed1.
24. Patel, V.; Ts, J.; Kamble, N.; Yadav, R.; K, T.; Pal, P.K.; Reddy Yc, J. Prevalence and Correlates of Psychiatric Comorbidity and Multimorbidity in Parkinson's Disease and Atypical Parkinsonian Syndromes. J. Geriatr. Psychiatry Neurol. 2023, 36, 155–163, doi:10.1177/08919887221103575.
25. Paul, B.S.; Aggarwal, S.; Paul, G.; Khehra, A.S.; Jain, A. Impulse-Control Disorders and Restless Leg Syndrome in Parkinson's Disease: Association or Coexistence. Ann. Indian Acad. Neurol. 2023, 26, 161–166, doi:10.4103/aian.aian_940_22.
26. Ferreri, F.; Agbokou, C.; Gauthier, S. Recognition and Management of Neuropsychiatric Complications in Parkinson's Disease. CMAJ 2006, 175, 1545–1552, doi:10.1503/cmaj.060542
27. Rosen, H.J.; Cummings, J. A Real Reason for Patients with Pseudobulbar Affect to Smile. Ann. Neurol. 2007, 61, 92–96, doi:10.1002/ana.21056.
28. Szatmari, S.; Illigens, B.M.-W.; Siepmann, T.; Pinter, A.; Takats, A.; Bereczki, D. Neuropsychiatric Symptoms in Untreated Parkinson's Disease. Neuropsychiatr. Dis. Treat. 2017, 13, 815–826, doi:10.2147/NDT.S130997.
29. Leroi, I.; Pantula, H.; McDonald, K.; Harbishettar, V. Neuropsychiatric Symptoms in Parkinson's Disease with Mild Cognitive Impairment and Dementia. Parkinsons Dis. 2012, 2012, 308097, doi:10.1155/2012/308097.
30. Alvarado-Bolaños, A.; Cervantes-Arriaga, A.; Rodríguez-Violante, M.; Llorens-Arenas, R.; Calderón-Fajardo, H.; Millán-Cepeda, R.; Leal-Ortega, R.; Estrada-Bellmann, I.; Zuñiga-Ramírez, C. Impact of Neuropsychiatric Symptoms on the Quality of Life of Subjects with Parkinson's Disease. J. Parkinsons. Dis. 2015, 5, 541–548, doi:10.3233/JPD-150597.
31. Pellicano, C.; Benincasa, D.; Pisani, V.; Buttarelli, F.R.; Giovannelli, M.; Pontieri, F.E. Prodromal Non-Motor Symptoms of Parkinson's Disease. Neuropsychiatr. Dis. Treat. 2007, 3, 145–152, doi:10.2147/nedt.2007.3.1.145.
32. van der Velden, R.M.J.; Broen, M.P.G.; Kuijf, M.L.; Leentjens, A.F.G. Frequency of Mood and Anxiety Fluctuations in Parkinson's Disease Patients with Motor Fluctuations: A Systematic Review: Mood and Anxiety Fluctuations in PD. Mov. Disord. 2018, 33, 1521–1527, doi:10.1002/mds.27465.
33. Blundell, E.K.; Grover, L.E.; Stott, J.; Schrag, A. The Experience of Anxiety for People with Parkinson's Disease. NPJ Parkinsons Dis. 2023, 9, 75, doi:10.1038/s41531-023-00512-1.
34. Kobylecki, C.; Carrasco, R.; Boca, M.; Lawton, M.; Chaudhuri, K.R.; Hu, M.T.; Grosset, D.G.; Silverdale, M.A. The Association between Pain and Impulse Control Behaviours in Parkinson's Disease. Parkinsonism Relat. Disord. 2020, 78, 53–55, doi:10.1016/j.parkreldis.2020.07.005.
35. Mercury, M.G.; Tschan, W.; Kehoe, R.; Kuechler, A. The Presence of Depression and Anxiety in Parkinson's Disease. Dis. Mon. 2007, 53, 296–301, doi:10.1016/j.disamonth.2007.03.001.
36. Sawada, H.; Umemura, A.; Kohsaka, M.; Tomita, S.; Park, K.; Oeda, T.; Yamamoto, K. Pharmacological Interventions for Anxiety in Parkinson's Disease Sufferers. Expert Opin. Pharmacother. 2018, 19, 1071–1076, doi:10.

1080/14656566.2018.1485650.
37. Yang, S.; Sajatovic, M.; Walter, B.L. Psychosocial Interventions for Depression and Anxiety in Parkinson's Disease. J. Geriatr. Psychiatry Neurol. 2012, 25, 113–121, doi:10.1177/0891988712445096.
38. Goetz, C.G.; Pappert, E.J.; Blasucci, L.M.; Stebbins, G.T.; Ling, Z.D.; Nora, M.V.; Carvey, P.M. Intravenous Levodopa in Hallucinating Parkinson's Disease Patients: High-Dose Challenge Does Not Precipitate Hallucinations. Neurology 1998, 50, 515–517, doi:10.1212/wnl.50.2.515.
39. Magdalinou, N.; Morris, H.R. Clinical Features and Differential Diagnosis of Parkinson's Disease. In Movement Disorders Curricula; Springer Vienna: Vienna, 2017; pp. 103–115 ISBN 9783709116272.
40. Bhugra, D. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 7th Edition (2 Vols). Behav. Res. Ther. 2002, 40, 1111, doi:10.1016/s0005-7967(01)00111-5.