



ORIGINAL ARTICLE

Affective and personality disorders in Parkinson's disease premotor phase. Pilot study.

Samushiya M.A.¹, Ragimova A.A.¹, Smolentseva I.G.², Maksimenko M.Yu.³, Ivannikova E.I.¹

¹ Central State Medical Academy of Department of Presidential Affairs, Moscow, Russia, ragimovaasia@gmail.com

² Central Clinical Hospital with polyclinic of Medical Center the Administrative, Department of the President of the Russian Federation, Moscow

³ Institute of Psychology named after L.S. Vygotsky, Federal State Budgetary Educational Institution of Higher Education Russian State University for the Humanities

Abstract

Neuropsychiatric symptoms are one of the factors determining quality of life among Parkinson's disease patients, but often remain underestimated by clinicians, especially in early disease stage. **Objective:** to study the clinical features of affective disorders and comorbid personality traits in prodrome of Parkinson's disease (PD) and their effect on treatment adherence. **Materials and methods:** 29 patients with PD were studied with questionnaires (Toronto alexithymia scale (TAS); Minicolumn personal questionnaire; DSM-IV criteria (SCID-II); Hospital anxiety and depression scale (HADS); Hamilton Scale for the Assessment of Depression (HAM-D)), and clinical-psychopathological method with objective information collection, neurological examination and neuropsychological testing. **Results:** Among the patients with PD, personality premorbid features cluster C were most prominent (48% patients). Affective disorders in the prodromal period of PD are dysthymia (13.7%); cyclothymia (6.8%); recurrent depressive disorder (34.4%); and single depressive episode (44.8%). Affective disorders in PD are characterized by late onset, the prevalence of anxiety, asthenic-apathetic symptoms, as well as a high level of alexithymia and somatization. We found the relationship of personality traits and adherence to therapy: the least compliant are histrionic $n = 3$ (10.3%) and schizotypal $n = 2$ (6.9%) patients. A high prevalence of dissociative reactions (55%) was noted in response to a diagnosis of PD, which is similar to cancer patients.

Keywords

Psychiatry, neurology, Parkinson's disease, psychoneurology

Parkinson's disease (PD) occurs in 0.5-5% of people over the age of 65 [1,2]. PD is a clinically heterogeneous disease that reflects the inhomogeneity of the sequence of involvement of brain structures in the degenerative process. [3,4]. Non-motor symptoms occur in 60% -100% of patients with PD [5]. According to a study by C. Juri (2006), there were non-motor disease manifestations in 81.5% of patients. Neuropsychiatric manifestations is present in 50.8% of patients: cognitive impairment - 30.6%, autonomic disturbance in 43.5%, and sleep impairment in 54.8% of patients [6]. Most common non-motor manifestations of PD are: anosmia, REM sleep behavior disorders, daytime sleepiness, gastrointestinal disorders, as well as a number of neuropsychiatric symptoms: anxiety, depression, personality traits changes [7]. Patients with PD with comorbid psychiatric symptoms (PPD) are more fragile than patients without it. In patients with PPD often observed paradoxical responses to medicines and delirium [8, 9].

There is increase in the frequency of seeking psychiatric care during the premotor phase of PD [10]. Despite the abundance of PPD, the attention of clinicians is focused on the motor sphere, and psychopathological symptoms remain unrecognized, due to the symptomatic "overlap" of psychiatric and motor complaints [11]. There are different views on the origin of PPD. On the one hand, there is an approach based on dividing symptoms depending on the

effect of dopaminergic therapy: symptoms of the "OFF" period (period of no drug action) and "ON" (period of drug action). [12].

On the other hand, according to the theory of H. Braak (2004), premotor symptoms in PD occur on average 17 years before the first motor symptoms appear due to damage to the nondopaminergic system of the brain and dysfunction of the mesocorticolimbic and striatal circuits [4, 7, 12, 13, 14].

Change in personality traits as a characteristic of premotor phase

Special "premorbid" personality traits characteristic of patients with PD have been observed by various authors since 1913: anancastic, dependent, paranoid and rigid dimensions are described, with low emotional intelligence and a tendency to "suppress" or displace emotional experiences [15, 16, 17, 18, 19, 20, 21, 22]. Similar characteristics were found in the working route of patients. Patients with PD better coped with organizational work, labor activities within the framework of regulated rules, were not inclined to creatively complete tasks, build theoretical concepts and deceit, were less likely to show career ambitions [23, 24, 25, 26, 27, 28, 29].

According to retrospective studies of objective history, patients with PD had traits of self-control, rigidity, introversion, dependence on the assessment and opinions of others and anxiety long before the first symptoms of parkinsonism appear [30, 31].

Parkinson personality is widely studied using different questionnaires: according to Big Five Model (BFM) questionnaire the most common characteristic was neurotism, while according to Cloninger Psychobiological Model (CPM) there was a decrease in novelty seeking and an increase in the harm avoidance [32, 33, 34]. Despite the abundance of works using the questionnaires described above, there is a rare use of tools to consider the “parkinsonian personality” in accordance to the DSM criteria [35]. According to A. Nicoletti (2013), it was found precedence of impulsive-compulsive traits in PD patients compared with the age-adjusted control group and its prevalence increased with increasing age and length of illness, which may indicate dysfunction of the fronto-striatal pathways before the onset of the disease [36, 37].

Personality PD characteristics have neuromediator correlates: the novelty seeking characteristic is associated with the dopaminergic system, harm avoidance is associated with serotonergic activity and the orbitofrontal, parietal and occipital cortex, reward dependence is associated with noradrenergic activity [38].

Changes in the novelty seeking function were also studied on model-based decision making theory [39]. When dopamine level rises in lateral prefrontal cortex, the likelihood of “habitual” actions is increased, and an increase in dopaminergic synapsis density in the ventral striatum increases model-free decision making [40; 41]. Disturbance in habitual behavior is considered to be involved in patients with PD. The machine learning model showed that “OFF” period determinates function of predicting a negative result, due to a decrease in the inhibitory effect of serotonin on the dopaminergic system of the brain [39, 43].

The premotor phase of PD is also characterized by a change in the subjective perception of own body, physical health, and one’s own abilities: patients with PD more often complain of weakness and fatigue, combined with a feeling of failure, inability to control both the body and one’s own will to act [42], that correlates with the mental status and disturbances in the visual analyzer, decrease in the feeling of loudness of one’s own voice and olfactory dysfunction [15; 42].

The factor determining the difficulty in diagnosing changes in mental state during the onset of the disease is alexithymia (difficulty in recognizing both own and extraneous emotions) - 26% in patients with diagnosed PD and 21% in patients at the initial stage of the disease [14]. The most common is the “frontal” theory of the origin of alexithymia, which is confirmed by the impairment of visual-spatial, executive, and non-verbal tasks during neurocognitive testing [42].

Anxiety and the spectrum of anxiety disorders

Anxiety is common at all stages of PD: from the premotor period to the advanced stages of the disease [11, 45, 46]. Even in the classic Essay on tremor palsy, J. Parkinson noted the importance of anxiety symptoms in the dynamics of PD [47].

Predisposing factors for the anxiety disorders in patients with PD are early onset of PD, male gender, postural instability, and high dosages of dopaminergic therapy. According to the results of epidemiological studies, patients with PD are more prone to

developing anxiety disorders and taking anxiolytic drugs before a diagnosis of PD [48]. The prevalence of anxiety disorders in patients with PD is up to 60%, however, anxiety remains unrecognized due to the similarity of symptoms with a neurological disease and comorbidity with depressive disorders - 92% of patients with PD with diagnosed anxiety showed a depressive disorder, and 62% of depressed patients with PD - Anxiety Disorder [11, 30, 49, 50]. Such overlap of symptoms is explained by a common neurobiological substrate: degeneration of the subcortical nuclei, dopamine, noradrenergic and serotonin pathways in the circuits, involving the fronto-basal ganglia, with a specific loss of dopaminergic and noradrenergic innervation in the locus coeruleus and limbic system of the brain [51]. The effect of anxiety on the PD quality of life and the patient’s adaptation is more significant than the cognitive decline: up to 67% of PD patients noted the negative impact of anxiety disorders on motor symptoms [52, 53, 54, 55]. Anxiety in PD manifested in 36% before the onset of the disease and in 64% after the diagnosis [56, 57]. In 42.5% of patients with PD, signs of social phobia were detected, while, in 8.8% before the manifestation of PD [58, 59].

Affective disorders

Prevalence of depression in PD is 20-35%, and the risk of occurrence became higher in 18% every year of the disease progression. A history of depressive disorders for 10 years is a significant risk factor for PD [59]. History of depression in patients with PD occurred in 9.2% compared with 4% in the control group [60, 61]. Risk factors for depressive disorders are female gender, severity of motor symptoms, difficulty in dosing dopaminergic drugs, decreased cognitive functions/dementia, psychotic episodes, anxiety and sleep disturbance [48]. A major depressive episode is more often observed before the manifestation of PD in 27.8%, dysthymia in 7.8%, and minor depression in 7.8% [57, 58]. As with the spectrum of anxiety disorders, clinical heterogeneity is noted depressive disorders in PD, in particular, an adjustment disorder is distinguished as a reaction to the diagnosis, a major depressive disorder, dysthymia [48]. There is a decrease in dopaminergic metabolism in the limbic system of the brain and thalamus, a decrease in the noradrenergic innervation of the blue nucleus, and a decrease in the serotonin innervation of the forebrain [52].

Hypomania and mania in the structure of bipolar disorder (BD), foreshadowing the manifestation of PD, is rare, however, there are data on isolated clinical cases in the literature [10, 62]. According to foreign literature, the prevalence of BD varies from 1% in the case of BD I and 5% in BD II, it is noteworthy that both manic and hypomanic episodes were recorded by patients or their caregivers only until the manifestation of motor symptoms and did not recur after the onset of dopaminergic therapy, in 3% of patients with BD hypomania changed to depression [63]. BD increases risk of disorders, impulse control, drug abuse, development of drug hypomania [64].

Schizophrenia

Both schizophrenia and PD impair the quality of life significantly [65]. Common to these diseases are: apathy, decreased motivation, ability to initiate action, altered emotional reactivity, which often do not reflect the dynamics of neurological disorders (or in the case of schizophrenia positive disorders), but have their own dynamics and portend the appearance of positive/motor symptoms.

Currently, there is no data on the prevalence of the spectrum of endogenous disorders in patients with PD. In a retrospective study of patients with PD, there is no association between schizophrenia and PD, however, in the study of patients in psychiatric clinics, there is an accumulation of patients with PD who, prior to the manifestation of motor symptoms, were treated on an outpatient basis or were hospitalized in a psychiatric hospital with a diagnosis of schizophrenia. [48].

Below are the results of our study of the characteristics of affective diseases in patients in premorbid BP, as well as their personality characteristics, preceding the appearance of motor symptoms of a neurological disease.

Aim: to study the clinical features of affective disorders and their comorbid personality traits manifesting in the prodrome of PD for 10-15 years before the diagnosis of PD, as well as their effect on adherence to treatment.

Methods: 29 patients up to 85 years in the absence of signs of obvious cognitive decline; 1-2.5 stage according to Hoehn-Yahr; the presence of affective disorders in the prodromal phase of PD for 0.5-10 years before the onset of motor signs of PD.

The study was based in the Federal State Institution "Clinical Hospital" of the Administrative Russian Federation President 's Department.

The study was conducted using questionnaires: Toronto Alexithymia Scale (TAS), Minimult questionnaire, DSM-IV Personal Questionnaire (SCID-II), Hospital Anxiety and Depression Scale (HADS), Hamilton Depression Rating Scale (HAM-D).

During the examination, psychiatrist, neuropsychological psychologist and neurologist examined all patients.

Sociodemographic data: 29 patients with a newly diagnosed PD a history of affective disorders was studied. The average age of patients was 69 ± 8.3 years; men $n = 14$ (48.2%), women $n = 15$ (51.8%). The stages of the disease according to Hoehn-Yahr: $n = 20$ (69%) - stage 2; $n = 9$ (31%) - 2.5 stage. Forms of PD disease: $n = 22$ - mixed form, $n = 3$ - tremulous form, $n = 4$ - akinetic-rigid form.

Neuropsychological examination

Neuropsychological examination revealed no dependence on the age or form of the disease. When performing the task of reciprocal hand coordination in all patients, except one, slight asymmetry is detected due to the left hand. In 12 patients (41.3%), there is an impairment of the simultaneous (simultaneous with something) method of processing information. All patients showed pathological inhibition and long-term memory impairment. At $n = 5$ (17.2%), there was a change in cause-effect relationships with the actualization of latent signs. In $n = 8$ (27.5%), there was an impairment of constructive praxis, and in 16 patients (55.1%) a decrease of auditory-speech memory.

In the group of patients with PD, personality premorbid features belonged mostly to C cluster (obsessive-compulsive and avoidant personalities) - 48%, which corresponds to previously published data.

Features of depression in the prodrome of BP

In patients with future PD onset of affective disorder was late (51 ± 3.7 years). Depression in the prodrome of PD had a high prevalence

of anxiety: health anxiety $n = 22$ (75.8%), anxiety for cognitive abilities $n = 8$ (27.5%), anxiety about symptoms of PD $n = 10$ (34.4%), anxiety about the general state of health $n = 4$ (13.7%), panic attacks $n = 5$ (17.2%). For many patients $n = 16$ (55.1%), feeling of self-change, a need for support by relatives was common.

The feeling of self-doubt was often combined with apathy and fatigue $n = 12$ (41.3%) and $n = 23$ (79.3%), respectively. A decrease in the ability to induce motivation $n = 14$ (48.2%) was also common in the prodromal period. Somatization and alexithymia were found both in personality premorbid characteristics and were traced in the structure of depression. According to the TAS characterological features of alexithymia were observed in $n = 15$ (52%), subclinical features in $n = 10$ (34%), no alexithymia was observed in $n = 4$ (14%). According to the HADS data, anxiety was found in $n = 29$ (100%), while depression at the time of examination was found only in $n = 14$ (48.3%). According to the HAMD (objective questionnaire), depression was observed at $n = 19$ (65.5%). A possible reason for the discrepancy is a high level of alexithymia and difficulty in recognizing emotions among patients with PD, which, however, requires further study in large samples. Among the studied patients in the prodrome of PD, the following variants of affective diseases were noted: dysthymia $n = 4$ (13.7%) cyclothymia $n = 2$ (6.8%) recurrent depressive disorder $n = 10$ (34.4%), the only depressive episode $n = 13$ (44.8%).

Dysthymia $n = 4$ (13.7%) duration 7 ± 2.2 years

Symptoms of dysthymia are comorbid to anxiety disorder (panic attacks and hypochondria anxiety). In all cases, it was high prevalence of somatization (palpitations, headaches, sleep disturbances, decreased appetite, constipation, flatulence, etc.) and a high risk of exacerbation of somatic diseases (gastritis, gastroduodenitis, retinal diseases weave, GB, periodontal disease, etc.).

Cyclothymia $n = 2$ (6.8%), duration 5 ± 2.3 years

The clinical picture of the depression episodes was represented by endoreactive symptom complexes (melancholy, anxiety with apathy and anhedonia), with a distinct daily rhythm (increased melancholy in the morning, sleep disturbance, loss of appetite). A psychogenic complex of depression is represented by loss of loved ones, divorce, etc. with persistent anxiety-phobic symptoms. Hypomania was presented by acceleration of associative and motor processes with a decrease in the need for sleep (up to 5-6 hours per day), increased working capacity but within the limits of conventional norms. In the structure of the last depressive episode (before the diagnosis of PD) there were florid astheno-dynamic disturbances.

Recurrent depressive disorder $n = 10$ (34.4%), duration 7 ± 3.2 years

In 10 cases (34.4%), psychopathological disorders manifested after a traumatic situation (relocation, divorce, death of a close relative, conflict at work, etc.). In 8 cases (27.6%) patients had 2 depressive episodes, in 2 cases (6.8%) - 3 episodes. The duration of the first depressive phase varied from 3 to 14 months (average 8.64 ± 2.39 months). In all cases, symptomatic remission of an average duration of $3.25 \text{ years} \pm 8.06$ months was observed. The average duration of the second depressive phase was 14.27 ± 3.6 months. The last depressive phase occurred 10 ± 3.70 months before the onset of the first motor symptoms.

The only depressive episode $n = 13$ (44.8%), duration 2 ± 0.7 years



The only depressive episode was reactive in nature and occurred after significant traumatic situations (death of a relative, dismissal from work, divorce), characterized by prevailing apathy with motor slowdown, loss of appetite, disruption of the digestive tract, rises in blood pressure, sleep disturbances, that are long perceived by clinicians as an affective, and not a neurological disease.

Personality features

The study also examined in detail the personality characteristics of patients with affective diseases in the prodrome of PD. Personality traits were investigated using the Minimult questionnaire and a personality questionnaire using the DSM-IV criteria (SCID-II).

Obsessive-compulsive personality disorder was recorded in $n = 13$ (44.8%) patients using SCID-II. Histrionic personality disorder was recorded in $n = 4$ (13.8%). Paranoid was $n = 3$ (10.3%), schizotypic - $n = 3$ (10.3%), schizoid - $n = 3$ (10.3%) and avoiding - $n = 3$ (10.3%).

The results of the Mini-Mult questionnaire (see Figure 1) generally confirm the data obtained using SCID-II with a peak on the psychasthenia scale. The second peak on the hypochondria scale does not characterize the individual as a trait, but the state of mental condition in response to the disease. Peaks on the scales of deceit and correction with a relatively low level of the reliability scale deserve a separate discussion. In light of the personality characteristics of patients with PD, it can be caused by tendency to give social acceptable answers and focus on social norms instead of tendency to lie itself.

An important consequence of the results is the fact that the identification of the personality characteristics of patients with PD should be carried out with the the clinical survey, which corrects the system biases of questionnaires results.

Sleep Disorders in PD

Before inclusion in the present study, sleep disorders were diagnosed in $n = 5$ (17.2%) patients; only $n = 2$ (6.8%) were treated for sleep disorders (see Figure 2). In a retrospective assessment, it was found that sleep disturbances manifested several years before the debut of BP - in 1-2 years in 12 cases (41.3%) and in 3-5 years in 10 cases (34.4%) ($n = 22$ (75.8%)), which allows us to consider them in some cases as one of the prodromal symptoms of PD.

At the time of examination, disturbances of night sleep were observed in most patients - $n = 24$ (82.7%). The structure of insomnia disorders in the studied sample was heterogeneous: $n = 11$ (38%), awakenings during the night and early awakenings in $n = 7$ (24%) and $n = 3$ (10.3%) respectively. Finally, in $n = 3$ (10.3%), according to patients and their relatives, symptoms related disturbances in the REM sleep phase were recorded: increased motor activity, lunacy and sleep talking.

Parkinson's disease diagnosis reaction

We found unexpectedly high prevalence of a dissociative reactions to the disease. In $n = 11$ (38%) mild dissociative reactions were recorded. Clinically such reactions were characterized by doubts about the seriousness of the diagnosis, attempts to convince themselves, relatives and doctors that the disease does not dangerous. In clinical examination of such patients still showed latent anxiety and affect lability - transient disturbances of falling

asleep, irritability, and selectively avoiding information about neurological pathology.

In $n = 5$ (17%), more severe dissociative reactions were detected, in the structure of which avoidance/procrastination phenomena were noted. Such patients rarely visited neurologists, mainly during hospitalization in a somatic hospital for another reason, but refused to believe in the diagnosis. Despite the presence of obvious neurological symptoms (falls, bradykinesia, tremors), they refused to take therapy in spite of the positive effect of their use.

The total prevalence of dissociation $n = 16$ (55%) in the sample of patients with PD significantly exceeds that for most somatic diseases and is comparable to oncological practice, where dissociation is most often recorded [68; 69]. Also noteworthy is the fact that all patients in the sample had a history of chronic somatic diseases (cardiovascular, gastroenterological), but even with their severity, none of the patients showed a dissociative response to them. In this regard, the high frequency of dissociation in PD cannot be explained only by the semantics and severity of neurological pathology, and this issue deserves further study.

Adherence to therapy

Adherence of PPD patients was low. Only $n = 17$ (58.6%) patients adhered to the recommended regimen for taking dopaminergic therapy. In $n = 12$ (41.3%), there were both missed treatment and manipulation of treatment with abuse of dopaminergic drugs. Moreover, patients with histrionic $n = 3$ (10.3%) and schizotypal personality traits $n = 2$ (6.9%) were most prone to abuse dopaminergic therapy. In the history of none of the patients with hysterical personality disorder, there was no significant abuse of alcohol or drugs, as well as non-chemical addictions. On the therapy none of the patients with hysterical trait had gambling or other behavioral disorders due to therapy (which may be due to the early stage of the disease and requires further observation)

Prescribed therapy after examination

At the time of examination, only $n = 5$ (17.2%) took psychopharmacotherapy (antidepressant, anti-anxiety drugs), the remaining patients $n = 24$ (82.7%) despite the presence of depression, insomnia and so on did not received psychopharmacotherapy. Psychopharmacotherapy was prescribed in 22 cases (75.8%), in two patients an improvement in mental status was due to correction of dopaminergic therapy. Patients were prescribed mainly antidepressants from the SSRI group (escitalopram, paroxetine) - $n = 11$ (38%), as well as trazadone (serotonin receptor antagonist / serotonin reuptake inhibitor) - $n = 11$ (38%). Quetiapine $n = 5$ (17.2%), was also used in small doses to correct anxiety disorders and insomnia.

Directions for future research:

1) In the future, we plan to distinguish a group of patients with comorbid mental pathology and Parkinson's disease to conduct a genetic study of the exon and/or to find common genetic features of Parkinson's and mental illness

2) We hope to expand the patient group to 200 for statistical confirmation of the materials received

3) We are going to identify specific traits of mental illnesses that occur in the prodrome of Parkinson's disease, allowing us to predict the imminent onset of a neurological disease.

4) We plan to compare specific personality traits and features of filling out the questionnaires with the control group

5) Some of the patients (up to 60) we plan to study in detail using a neuropsychological study to identify specific neuropsychological markers of patients with Parkinson's disease and mental illness

References

- Schapira, A.H.V., Chaudhuri, K.R., Jenner P.(2017). Non-motor features of Parkinson disease. *Nature Reviews Neuroscience*, 18(8):509-509. <https://doi:10.1038/nrn.2017.91>.
- Rijk, M.C.D., Tzourio, C., Breteler, M.M., et al.(1997). Prevalence of parkinsonism and Parkinsons disease in Europe: the EUROPARKINSON Collaborative Study. *European Community Concerted Action on the Epidemiology of Parkinsons disease. Journal of Neurology, Neurosurgery & Psychiatry*, 62(1):10-15. <https://doi:10.1136/jnnp.62.1.10>.
- Klein, J., Rolinski, M., Griffanti, L., et al.(2018). Cortical structural involvement and cognitive dysfunction in early Parkinsons disease. *NMR in Biomedicine*, 31(4). <https://doi:10.1002/nbm.3900>.
- Braak, H., Ghebremedhin, E., Rüb, U., Bratzke, H., Tredici, K.D.(2004). Stages in the development of Parkinson's disease-related pathology. *Cell and Tissue Research*, 318(1):121-134. <https://doi:10.1007/s00441-004-0956-9>.
- Khagai, O., Selyanina, N.(2018). Comparative characteristics of non-motor manifestations of Parkinson disease in men and women. *Medical almanac*. <https://doi:10.21145/2499-9954-2018-5-120-122>.
- Juri, C.C., Chaná, C.P.(2006). Levodopa for Parkinson's disease: What have we learned? *Rev Med Chil*, 134(7):893-901. Epub 2006 Aug 29. PMID 17130974
- Chahine, L.M., Stern, M.B.(2014). Characterizing Premotor Parkinsons Disease: Clinical Features and Objective Markers. *Movement Disorders Clinical Practice*, 1(4):299-306. <https://doi:10.1002/mdc3.12062>.
- Chiu, P.-Y., Tsai, C.-T., Chen, P.-K., Chen, W.-J., Lai, T.-J.(2016). Neuropsychiatric Symptoms in Parkinson's Disease Dementia Are More Similar to Alzheimer's Disease than Dementia with Lewy Bodies: A Case-Control Study. *Plos One*, 11(4). <https://doi:10.1371/journal.pone.0153989>.
- Lubomski, M., Rushworth, R.L., Tisch, S.(2014). Hospitalisation and comorbidities in Parkinsons disease: a large Australian retrospective study. *Journal of Neurology, Neurosurgery & Psychiatry*, 86(3):324-330. <https://doi:10.1136/jnnp-2014-307822>.
- Lin, H.-L., Lin, H.-C., Chen, Y.-H.(2014). Psychiatric diseases predated the occurrence of Parkinson disease: a retrospective cohort study. *Annals of Epidemiology*, 24(3):206-213. <https://doi:10.1016/j.annepidem.2013.12.010>.
- Han, J.W., Ahn, Y.D., Kim, W.-S., et al.(2018). Psychiatric Manifestation in Patients with Parkinsons Disease. *Journal of Korean Medical Science*, 33(47). <https://doi:10.3346/jkms.2018.33.e300>.
- Fuente-Fernández, R.D.L.(2013). Imaging of Dopamine in PD and Implications for Motor and Neuropsychiatric Manifestations of PD. *Frontiers in Neurology*, 4. <https://doi:10.3389/fneur.2013.00090>.
- Kim, S.R., Nho, J.-H., Nam, J.-H.(2017). Relationships among Type-D personality, symptoms and quality of life in patients with ovarian cancer receiving chemotherapy. *Journal of Psychosomatic Obstetrics & Gynecology*, 39(4):289-296. <https://doi:10.1080/0167482x.2017.1372416>.
- Poletti, M., Frosini, D., Pagni, C., et al.(2011). Alexithymia Is Associated with Depression in de novo Parkinson's Disease. *Psychotherapy and Psychosomatics*, 80(4):251-253. <https://doi:10.1159/000322029>.
- Sozinova, E.V.(2010). Parkinson's Patient Identity. *Nervous Disease Treatment*, 1(3): 29-33 (In Russ)
- Poewe W.(1990). The premorbid personality of patients with Parkinson's disease. *New Vistas in Drug Research Early Markers in Parkinson's and Alzheimer's Diseases*. 23-30. <https://doi:10.1007/978-3-7091-9098-2_4>.
- Lit, A.C.(1968). Man behind a mask. An analysis of the psychomotor phenomena of Parkinsons disease. *Acta Neurol. Belg*, 68:863-874. PMID 4976734
- Machover, S.(1957). Rorschach Study on the Nature and Origin of Common Factors in the Personalities of Parkinsonians. *Psychosomatic Medicine*, 19(4):332-338. <https://doi.org/10.1097/00006842-195707000-00010>.
- Prichard, J.S., Schwab, R.S., Tillmann, W.A.(1951). The Effects of Stress and the Results of Medication in Different Personalities with Parkinson's Disease. *Psychosomatic Medicine*, 13(2):106-111. <https://doi.org/10.1097/00006842-195103000-00003>.
- Booth, G.(1948). Psychodynamics in Parkinsonism. *Psychosomatic Medicine*, 10(1):1-14. <https://doi.org/10.1097/00006842-194801000-00001>.
- Sands, I.J.(1942). The type of personality susceptible to Parkinson's disease. *J. Mt. Sinai Hosp*, 9: 792-794. PMID 10911877
- Jelliffe, S.E.(1940). The Parkinsonian Body Posture. *The Journal of Nervous and Mental Disease*, 91(5):663. <https://doi:10.1097/00005053-194005000-00030>.
- Sullivan, K.L., Mortimer, J.A., Wang, W., Zesiewicz, T.A., Brownlee, H., Borenstein, A.R.(2015). Occupational Characteristics and Patterns as Risk Factors for Parkinson's Disease: A Case Control Study. *Journal of Parkinsons Disease*, 5(4):813-820. <https://doi.org/10.3233/jpd-150635>.
- Rosen, J.B., Brand, M., Polzer, C., Ebersbach, G., Kalbe, E.(2013). Moral decision-making and theory of mind in patients with idiopathic Parkinson's disease. *Neuropsychology*, 27(5):562-572. <https://doi.org/10.1037/a0033595>.
- Gatto, N.M., Bordelon, Y., Gatz, M., Ritz, B.(2011). Personality Characteristics and Motor Skills Attributed to Occupations in Parkinson Disease. *Cognitive and Behavioral Neurology*, 24(1):18-25. <https://doi:10.1097/wnn.0b013e318218c5eb>.
- Abe, N., Fujii, T., Hirayama, K., et al.(2009). Do parkinsonian patients have trouble telling lies? The neurobiological basis of deceptive behaviour. *Brain*, 132(5):1386-1395. <https://doi.org/10.1093/brain/awp052>.
- Schneider, J.S.(2007). Behavioral persistence deficit in Parkinsons disease patients. *European Journal of Neurology*,



- 14(3):300-304. <<https://doi.org/10.1111/j.1468-1331.2006.01647.x>>.
28. Hooker, C., Roese, N.J., Park, S.(2000). Impoverished Counterfactual Thinking is Associated with Schizophrenia. *Psychiatry*, 63(4):326-335. <<https://doi.org/10.1080/00332747.2000.11024925>>.
29. Ward, C.D., Duvoisin, R.C., Ince, S.E., Nutt, J.D., Eldridge, R., Calne, D.B.(1983). Parkinsons disease in 65 pairs of twins and in a set of quadruplets. *Neurology*, 33(7):815-815. <<https://doi.org/10.1212/wnl.33.7.815>>.
30. Menza, M.A., Robertson-Hoffman, D.E., Bonapace, A.S.(1993). Parkinsons disease and anxiety: Comorbidity with depression. *Biological Psychiatry*, 34(7):465-470. <[https://doi.org/10.1016/0006-3223\(93\)90237-8](https://doi.org/10.1016/0006-3223(93)90237-8)>.
31. Duvoisin, R.C., Eldridge, R., Williams, A., Nutt, J., Calne, D.(1981). Twin study of Parkinson disease. *Neurology*, 31(1):77-77. <<https://doi.org/10.1212/wnl.31.1.77>>.
32. Cerasa A.(2018). Re-examining the Parkinsonian Personality hypothesis: A systematic review. *Personality and Individual Differences*, 130:41-50. <<https://doi.org/10.1016/j.paid.2018.03.045>>.
33. Baig, F., Lawton, M.A., Rolinski, M., et al.(2017). Personality and addictive behaviours in early Parkinsons disease and REM sleep behaviour disorder. *Parkinsonism & Related Disorders*, 37:72-78. <<https://doi.org/10.1016/j.parkreldis.2017.01.017>>.
34. Volpato, C., Signorini, M., Meneghello, F., Semenza, C.(2009). Cognitive and Personality Features in Parkinson Disease: 2 Sides of the Same Coin? *Cognitive and Behavioral Neurology*, 22(4):258-263. <<https://doi.org/10.1097/wnn.0b013e3181c12c63>>.
35. Luca, A., Nicoletti, A., Mostile, G., Zappia, M.(2019). The Parkinsonian Personality: More Than Just a "Trait." *Frontiers in Neurology*, 9. <<https://doi.org/10.3389/fneur.2018.01191>>.
36. Nicoletti, A., Luca, A., Raciti, L., et al.(2013). Obsessive Compulsive Personality Disorder and Parkinson's Disease. *PLoS ONE*, 8(1). <<https://doi.org/10.1371/journal.pone.0054822>>.
37. Fineberg, N.A., Potenza, M.N., Chamberlain, S.R., et al.(2009). Probing Compulsive and Impulsive Behaviors, from Animal Models to Endophenotypes: A Narrative Review. *Neuropsychopharmacology*, 35(3):591-604. <<https://doi.org/10.1038/npp.2009.185>>.
38. Stallings, M.C., Hewitt, J.K., Cloninger, C.R., Heath, A.C., Eaves, L.J.(1996). Genetic and environmental structure of the Tridimensional Personality Questionnaire: Three or four temperament dimensions? *Journal of Personality and Social Psychology*, 70(1):127-140. <<https://doi.org/10.1037/0022-3514.70.1.127>>.
39. Heinz, A.(2017). A New Understanding of Mental Disorders: Computational Models for Dimensional Psychiatry. Cambridge, MA: MIT press.
40. Wunderink, L., Nieboer, R.M., Wiersma, D., Sytema, S., Nienhuis, F.J.(2013). Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment Strategy. *JAMA Psychiatry*, 70(9):913. <<https://doi.org/10.1001/jamapsychiatry.2013.19>>.
41. Deserno, L., Huys, Q.J.M., Boehme, R., et al.(2015). Ventral striatal dopamine reflects behavioral and neural signatures of model-based control during sequential decision making. *Proceedings of the National Academy of Sciences*, 112(5):1595-1600. <<https://doi.org/10.1073/pnas.1417219112>>.
42. Costa, A., Peppe, A., Carlesimo, G.A., Pasqualetti, P., Caltagirone, C.(2006). Alexithymia in Parkinsons disease is related to severity of depressive symptoms. *European Journal of Neurology*, 13(8):836-841. <<https://doi.org/10.1111/j.1468-1331.2006.01216.x>>.
43. Sharp, M.E., Foerde, K., Daw, N.D., Shohamy, D.(2015). Dopamine selectively remediates 'model-based' reward learning: a computational approach. *Brain*, 139(2):355-364. <<https://doi.org/10.1093/brain/awv347>>.
44. Sieurin, J., Gustavsson, P., Weibull, C.E., et al.(2015). Personality traits and the risk for Parkinson disease: a prospective study. *European Journal of Epidemiology*, 31(2):169-175. <<https://doi.org/10.1007/s10654-015-0062-1>>.
45. Lahey, B.B. (2009). Public health significance of neuroticism. *American Psychologist*, 64(4):241-256. <<https://doi.org/10.1037/a0015309>>.
46. Bell, I.R., Amend, D., Kaszniak, A.W., et al.(1995). Trait shyness in the elderly: evidence for an association with Parkinson's disease in family members and biochemical correlates. *J Geriatr Psychiatry Neurol*, 8:16-22 PMID: 7710641
47. Chen, J.J., Marsh L.(2013). Anxiety in Parkinson's disease: identification and management. *Therapeutic Advances in Neurological Disorders*, 7(1):52-59. <<https://doi.org/10.1177/1756285613495723>>.
48. Weisskopf, M.G., Chen, H., Schwarzschild, M.A., Kawachi, I., Ascherio, A.(2003). Prospective study of phobic anxiety and risk of Parkinsons disease. *Movement Disorders*, 18(6):646-651. <<https://doi.org/10.1002/mds.10425>>.
49. Valli, M., Mihaescu, A., Strafella, A.P.(2017). Imaging behavioural complications of Parkinson's disease. *Brain Imaging and Behavior*, 13(2):323-332. <<https://doi.org/10.1007/s11682-017-9764-1>>.
50. Broen, M.P.G., Narayan, N.E., Kuijf, M.L., Dissanayaka, N.N.W., Leentjens, A.F.G.(2016). Prevalence of anxiety in Parkinsons disease: A systematic review and meta-analysis. *Movement Disorders*, 31(8):1125-1133. <<https://doi.org/10.1002/mds.26643>>.
51. Remy, P., Doder, M., Lees, A., Turjanski, N., Brooks, D.(2005). Depression in Parkinsons disease: loss of dopamine and noradrenaline innervation in the limbic system. *Brain*, 128(6):1314-1322. <<https://doi.org/10.1093/brain/awh445>>.
52. Wiesli, D., Meyer, A., Fuhr, P., Gschwandtner, U.(2017). Influence of Mild Cognitive Impairment, Depression, and Anxiety on the Quality of Life of Patients with Parkinson Disease. *Dementia and Geriatric Cognitive Disorders Extra*, 7(3):297-308. <<https://doi.org/10.1159/000478849>>.
53. Siciliano, M., Trojano, L., Micco, R.D., et al.(2017). Motor, behavioural, and cognitive correlates of fatigue in early, de novo Parkinson disease patients. *Parkinsonism & Related Disorders*, 45:63-68. <<https://doi.org/10.1016/j.parkreldis.2017.10.004>>.
54. Carrozzino, D., Morberg, B.M., Siri, C., Pezzoli, G., Bech, P.(2018). Evaluating psychiatric symptoms in Parkinsons Disease by a clinimetric analysis of the Hopkins Symptom Checklist (SCL-90-R). *Progress in Neuro-Psychopharmacology and Biological*

- Psychiatry, 81:131-137.
<<https://doi.org/10.1016/j.pnpb.2017.10.024>>.
55. Timpka, J., Svensson, J., Nilsson, M.H., Pålhagen, S., Hagell, P., Odin, P.(2016). Workforce unavailability in Parkinsons disease. *Acta Neurologica Scandinavica*, 135(3):332-338.
<<https://doi.org/10.1111/ane.12602>>.
 56. Dissanayaka, N.N.W., White, E., O'Sullivan, J.D., Marsh, R., Pachana, N.A., Byrne, G.J.(2014). The clinical spectrum of anxiety in Parkinson's disease. *Movement Disorders*. 17.
<<https://doi.org/10.1002/nbm.3900>>.
 57. Dissanayaka, N.N.W., Osullivan, J.D., Pachana, N.A., et al.(2016). Disease-specific anxiety symptomatology in Parkinsons disease. *International Psychogeriatrics*, 28(7):1153-1163.
<<https://doi.org/10.1017/s1041610215002410>>.
 58. Ozdilek, F.B., Bestepe, E.E., Gultekin, B.K.(2014). Social phobia in Parkinson's disease: Prevalence and risk factors. *Neuropsychiatric Disease and Treatment*, 829.
<<https://doi.org/10.2147/ndt.s62942>>.
 59. Behari, M., Srivastava, A.K., Das, R.R., Pandey, R.(2001). Risk factors of Parkinsons disease in Indian patients. *Journal of the Neurological Sciences*, 190(1-2):49-55.
<[https://doi.org/10.1016/s0022-510x\(01\)00578-0](https://doi.org/10.1016/s0022-510x(01)00578-0)>.
 60. Leentjens, A.F., Akker, M.V.D., Metsemakers, J.F., Lousberg, R., Verhey, F.R.(2003). Higher incidence of depression preceding the onset of Parkinsons disease: A register study. *Movement Disorders*, 18(4):414-418. <<https://doi.org/10.1002/mds.10387>>.
 61. Schuurman, A.G., Akker, M.V.D., Ensink, K.T., et al.(2002). Increased risk of Parkinsons disease after depression: A retrospective cohort study. *Neurology*, 58(10):1501-1504.
<<https://doi.org/10.1212/wnl.58.10.1501>>.
 62. Novaretti, T.M., Novaretti, N., Tumas, V.(2016). Bipolar disorder, a precursor of Parkinsons disease? *Dementia & Neuropsychologia*, 10(4):361-364.
<<https://doi.org/10.1590/s1980-5764-2016dn1004018>>.
 63. Kummer, A., Dias, F.M.V., Cardoso, F., Teixeira, A.L.(2010). Low frequency of bipolar disorder, dopamine dysregulation syndrome, and punding in Brazilian patients with Parkinsons disease. *Revista Brasileira de Psiquiatria*, 32(1):62-65.
<<https://doi.org/10.1590/s1516-44462010000100012>>.
 64. Weintraub, D., David, A.S., Evans, A.H., Grant, J.E., Stacy, M.(2014). Clinical spectrum of impulse control disorders in Parkinsons disease. *Movement Disorders*, 30(2):121-127.
<<https://doi.org/10.1002/mds.26016>>.
 65. Andlin-Sobocki, P., Rossler, W.(2005). Cost of psychotic disorders in Europe. *European Journal of Neurology*, 12:74-77.
<<https://doi.org/10.1111/j.1468-1331.2005.01198.x>>.
 66. Winograd-Gurvich, C., Fitzgerald, P., Georgiou-Karistianis, N., Bradshaw, J., White O.(2006). Negative symptoms: A review of schizophrenia, melancholic depression and Parkinsons disease. *Brain Research Bulletin*, 70(4-6):312-321.
<<https://doi.org/10.1016/j.brainresbull.2006.06.007>>.
 67. Pläschke, R.N., Cieslik, E.C., Müller, V.I., et al.(2017). On the integrity of functional brain networks in schizophrenia, Parkinsons disease, and advanced age: Evidence from connectivity-based single-subject classification. *Human Brain Mapping*, 38(12):5845-5858.
<<https://doi.org/10.1002/hbm.23763>>.
 68. Smulevich A. B., Ivanov S. V., Myasnikova L. K., Dvoynikov S. YU., Samushiya M. A., Petelin D. S.(2014). Dissociative disorders in oncology: psychopathology, aspects of comorbidity with personality disorders. *Mental disorders in general medicine*, 3-4:4-14 (In Russ).
 69. Ivanov S. V., Petelin D. S.(2016). Typology of nosogenic reactions with the phenomena of autoaggression (procrastination phenomenon) in malignant neoplasms. *Mental disorders in general medicine*, 3:17-25 (In Russ).

Received: 11. 9. 2019

Accepted: 31.12. 20119

Figure 1. Average values of the Mini-Mult.

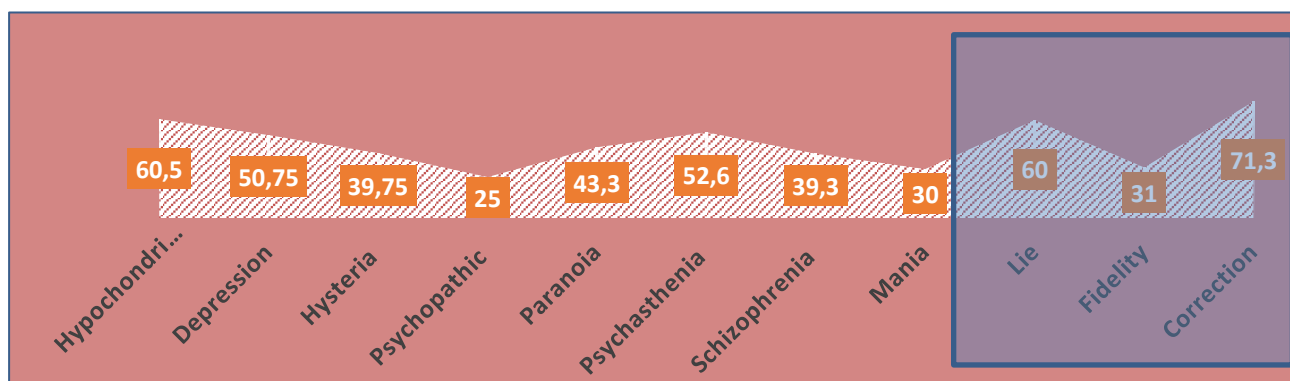


Figure 2. The occurrence of sleep disorders before PD

