

COMMENTARY TO HABILITATION THESIS¹

PSYCHOPHARMACOLOGICAL AND CLINICAL CORRELATES OF AFFECTIVE DISORDERS: A SCIENTIFIC RESEARCH PERSPECTIVE IN PSYCHIATRY

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Brief characteristic of the investigated matter

Affective disorders, whose common feature is primarily a pathological mood disorder, bring extraordinary suffering, tend to recur or occur chronically, occur at any age, affect millions of people worldwide, represent not only an important medical, but also a social and economic problem. The treatment of affective disorders should always be comprehensive, with the representation of biological and non-biological therapeutic procedures in various phases of treatment. The basic pillar of biological treatment of these disorders is pharmacotherapy, in indicated cases electroconvulsive therapy, repetitive transcranial magnetic stimulation, and some other procedures are also used. Psychotherapy as a non-biological therapeutic method is one of the standard treatment procedures for affective disorders. The occurrence of affective disorders is associated with several psychiatric comorbidities. In depressive disorders, the anxiety disorders, dysthymia, PTSD and a higher risk of suicidal behaviour are most often found. In addition, somatic comorbidities include dorsopathies, hypertension, metabolic diseases, as well as migraine, multiple sclerosis and sleep disorders. Complications and comorbidities of affective disorders are a significantly problematic topic, mainly due to their chronic course and the frequent occurrence.

Objectives of the work and employed methodologies

The submitted habilitation thesis consists of a set of published works on diagnosis, therapy, complications and comorbidities of affective disorders, which are supplemented with brief commentaries. The first part of the work is an introduction to the issue of affective disorders related to epidemiology, etiopathogenesis, therapy and finally their complications and comorbidities. Data from the Health Information Center of the Slovak Republic for 2022 show that of all mental disorders, affective disorders were the most common reason for seeking psychiatric help (31.4%) and the third most common reason for hospitalization (14.5%). The goal of treating depression is to achieve remission and subsequent recovery. Affective disorders also significantly affect the health

¹The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

and social system. The total annual costs for patients with affective disorders in Slovakia represent more than 71 million euros. Untreated patients are also a problem. In Slovakia, on average, only one in five people with an affective disorder is diagnosed and adequately treated. The second part of the habilitation thesis is primarily devoted to complications and comorbidities of affective disorders through the possibilities of innovative diagnostics, emphasizing the importance of pharmacological treatment of depressive disorders and at the same time the little-known role of autogenic training in mental disorders. Any possibility of revealing a reduction in the risk of complications and comorbidities of affective disorders in connection with suicidality, cardiovascular risk or diabetes has the potential to improve the quality of life and reduce morbidity and mortality of people with affective disorders. The habilitation thesis can thus enrich the current and future horizons of long-term sustainable complex individualized management of affective disorders.

Obtained results

The habilitation work consists of selected publications from three areas: i) diagnosis of affective disorders, ii) therapy of affective disorders, and iii) complications and comorbidities of affective disorders.

i) The presented publication in the field of diagnostics [1] highlights original innovative diagnostic possibilities for depressive disorders. The results showed that the proteome of human tear fluid could be helpful in distinguishing between a group of individuals with depressive disorders and healthy controls [1]. The identification of subtle neurobiological abnormalities in depressive disorders could be clinically useful in predictive, preventive and personalized medicine and serve as a basis for further research into depressive disorders in psychiatry [1].

ii) In a randomized comparative, pragmatic study of patients with a non-psychotic moderate or severe depressive episode [2], the effects and impact of implementing a structured psychoeducational intervention on the clinical course of depressive disorder prospectively over a two-year period were primarily investigated. The results show that a psychoeducational intervention based on a modified Munoz course of depression prevention has beneficial effects in adults with depressive disorder even after inpatient psychiatric treatment and may offer a new approach in preventing relapses of depressive disorder [2].

Within the framework of the therapy of affective disorders, we emphasize the importance of comprehensive treatment, and thus the little-known role of autogenic training in affective disorders [3]. As a complementary interventional psychotherapeutic technique with a favorable outcome on psychophysiological functioning, the autogenic training represents a promising path to expanding

research knowledge about the brain-body connection beyond the current boundaries of prevention and clinical management of many mental disorders [3].

According to generally accepted recommendations, antidepressants should not be the first-line drug for the treatment of mild depression. In the treatment of moderate and severe depressive disorders, antidepressants are the first-line drugs. We published a textbook [4] to guide the treatment of psychiatric and somatic comorbidities, along with the assessment of a suicidal risk and patient compliance.

The contribution of antidepressants and the causal contribution of depressive disorder in the etiopathogenesis of dyslipidemias are currently not sufficiently clarified. In our study [5], we reported that compared to older antidepressants, the SSRI drugs did not worsen lipid parameters, especially triglycerides.

The results of our cross-sectional quantitative-qualitative analysis show that the legislatively anchored standard diagnostic and therapeutic procedures for depressive disorders in Slovakia, including standard monitoring of laboratory parameters, are well implemented [6].

Through a first report of the use of the continuous glucose monitoring in bipolar disorder and type 1 diabetes mellitus, we reveal unrecognized glycemic fluctuations in unmedicated vs. medicated disorders, highlighting the metabolic benefits of antipsychotics [7]. The selection of psychotropic drugs with a neutral metabolic effect and individualization of the dose hold significant promise for the optimization of antipsychotic and antidiabetic therapy [7].

iii) Complications and comorbidities of affective disorders are a significantly problematic and burning topic, mainly due to their chronic course and the high probability of their occurrence. In relation to suicidal behaviour in patients with bipolar disorder, we found that suicidal thoughts and attempts occurred three times more often in women and we identified up to four times higher incidence of suicidal attempts in women with bipolar disorder without lithium treatment compared to women treated by lithium [8].

The key conditions for effective modification and reduction of cardiovascular risk in psychiatry comprise the interdisciplinary care, regular screening for cardio-metabolic diseases, their early diagnosis and effective and safe individualized therapy. With respect to a comprehensive management of affective disorders, we have identified a need for a closer collaboration between cardiologists and psychiatrists [9, 10].

The observed bidirectional interaction in our narrative review [11] merits a screening for psychiatric disorders in type 2 DM and vice versa to allow for early detection and treatment of this at-risk population. Selection of drugs with neutral metabolic effects and dose individualization hold significant promise for optimizing therapy with antipsychotic and antidiabetic agents [11].

The aim of the next paper was to critically describe the situation after more than two years of the COVID-19 pandemic and to evaluate the impact and diversity of the effects of pandemic stress on mental health outcomes of people with diabetes (mental health disorder screening, suicidal ideation, generalized anxiety symptoms, depressive symptoms)[12]. The paper also analyzes the development of new individualized therapeutic approaches and treatment strategies to mitigate the negative psychological impact of the COVID-19 pandemic on diabetes [12].

Within Slovakia, we identified the pathological impact of the COVID-19 pandemic mainly in patients with affective and anxiety disorders and the occurrence of the pathological impact of the COVID-19 pandemic on the mental state of healthcare workers mainly in the form of personal and work stress[13]. Psychosocial support in Slovakia was newly organized within the framework of the COVID-19 pandemic for healthcare workers, patients and other residents under high stress in a very short time. This unexpected situation revealed the need for reform of the psychiatric care system in Slovakia, which we initiated by publishing the basic principles of psychiatric care in Slovakia [13].

The presented results can enrich the current and future horizons of long-term sustainable comprehensive individualized management of affective disorders, not only in terms of symptoms, but especially in improving the overall quality of life and functioning of people with affective disorders.

Applicant's contribution

Of the 13 published articles included in the thesis, the applicant was the first and/or the corresponding author of 9 (69%). In the biomedical-genetic oriented article where the first author was a biomedical specialist, the applicant closely collaborated with the first author and provided clinical and medical background to the research. The applicant wrote two articles with colleagues in a shared first authorship.

Bibliographic record of published scientific results included in the habilitation thesis Accessibility and Web of Science (WoS) classifications

[1]KRAJCIKOVA, Kristina, Erika SEMANCIKOVA, Katarina ZAKUTANSKA, Daria KONDRAKHOVA, Jana MASLANKOVA, Marek STUPAK, Ivan TALIAN, Natalia TOMASOVICOVA, Tatiana KIMAKOVA, Vladimir KOMANICKY, Katarina DUBAYOVA, **Dagmar BREZNOSCAKOVA**, Eva PALOVA, Juraj SEMANCIK and Vladimira TOMECKOVA. Tear fluid biomarkers in major depressive disorder: Potential of spectral methods in biomarker discovery. *Journal of Psychiatric Research* [online]. 2021, **138**, 75–82. ISSN 1879-1379. Available at: doi:10.1016/j.jpsychires.2021.03.038

Document Type: Article; IF = 5,250; median IF PSYCHIATRY – SSCI 3,411; according to IF PSYCHIATRY Q2; according to AIS PSYCHIATRY – SSCI Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60	60	20	30

[2]**BREZNOSCAKOVA, Dagmar**, Maria PALLAYOVA, Lubomira IZAKOVA and Maria KRALOVA. In-person psychoeducational intervention to reduce hospitalizations and improve the clinical course of major depressive disorder: a non-randomized pilot study. *Frontiers in Psychiatry* [online]. 2024, **15**(Article 1429913). ISSN 1664-0640. Available at: doi:10.3389/fpsyt.2024.1429913

Document Type: Article; in 2023 IF = 3,200; median IF PSYCHIATRY – SSCI 2,450; according to IF PSYCHIATRY Q2; according to AIS PSYCHIATRY – SSCI Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60	55	65	75

[3]**BREZNOSCAKOVA, Dagmar**, Milana KOVANICOVA, Eva SEDLAKOVA and Maria PALLAYOVA. Autogenic Training in Mental Disorders: What Can We Expect? *International Journal of Environmental Research and Public Health* [online]. 2023, **20**(5, Article number 4344). ISSN 1661-7827. Available at: doi:10.3390/ijerph20054344

Document Type: Review; Category: Health, Toxicology and Mutagenesis – SJR Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40	30	60	55

[4]PÁLOVÁ, Eva a **Dagmar BREZNOŠČÁKOVÁ**. Farmakologická liečba depresívnych porúch. In: Ladislav MIROSSAY a Ján MOJŽIŠ. *Základná farmakológia a farmakoterapia II.* 2., rev. a rozš. vyd. Košice: Equilibria, 2021, s. 947-956. ISBN 978-80-8143-273-6.

WoS listing without impact factor

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	55	50	60

[5]**BREZNOŠČÁKOVÁ, Dagmar**, Martina CHYLOVÁ and Klára MACEKOVÁ. Vplyv antidepresív na lipidový profil. *Psychiatria pre prax.* 2011, **12**(4), 157-159. ISSN 1335-9584.

Original publication. WoS listing without impact factor, article published in another peer-reviewed journal

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
85	70	75	80

[6]KRÁLOVÁ, Mária and **Dagmar BREZNOŠČÁKOVÁ**. Klinický manažment pacienta s depresívnou epizódou v súčasnej psychiatrickej praxi [Clinical management of a patient with depressive episode in current psychiatric practice]. *Psychiatria pre prax*. 2022, **23**(3), 118-124. ISSN 1335-9584.

Original publication. WoS listing without impact factor, article published in another peer-reviewed journal

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	45	40	50

[7]**BREZNOSCAKOVA, Dagmar** and Maria PALLAYOVA. Case report: Uncovering hidden glucose patterns in medicated versus unmedicated bipolar disorder and comorbid type 1 diabetes mellitus. *Frontiers in Endocrinology* [online]. 2024, **15**(Article 1354749). ISSN 1664-2392. Available at: doi:10.3389/fendo.2024.1354749

Document Type: Article; in 2023 IF = 3,900; median IF ENDOCRINOLOGY & METABOLISM – SCIE 2,900; according to IF ENDOCRINOLOGY & METABOLISM Q2; according to AIS ENDOCRINOLOGY & METABOLISM – SCIE Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	45	40	50

[8]**BREZNOŠČÁKOVÁ, Dagmar**, Eva PÁLOVÁ, Boris BODNÁR, Jozef DRAGAŠEK, Anna ČORBOVÁ and Klára LOŠONCIOVÁ. Suicidalita u hospitalizovaných pacientov s bipolárnou afektívnou poruchou (10-ročné sledovanie). *Psychiatria pre prax*. 2009, **10**(1), 29-31. ISSN 1335-9584.

Original publication. WoS listing without impact factor, article published in another peer-reviewed journal

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40	45	60	55

[9]**BREZNOŠČÁKOVÁ Dagmar** and Mária PALLAYOVÁ. Kardiovaskulárne riziko v psychiatrii. *Kapitoly z kardiologie pro praktické lékaře*. 2023, **15**(1), 23-30. Reprint s. R1-R7. ISSN 1803-7542.

Original publication. WoS listing without impact factor, article published in another peer-reviewed journal

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	45	40	50

[10]**BREZNOŠČÁKOVÁ, Dagmar** and Lenka KAMENICKÁ. Výskyt depresívnych a úzkostných symptómov u pacientov s kardiovaskulárnym ochorením. *Psychiatria pre prax*. 2013, **14**(4), 164-167. ISSN 1335-9584.

Original publication. WoS listing without impact factor, article published in another peer-reviewed journal

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60	75	70	65

[11]**BREZNOSCAKOVA, Dagmar** and Maria PALLAYOVA. Bipolar disorder and type 2 diabetes mellitus: A bidirectional relationship. *European Journal of Psychiatry* [online]. 2022, **36**(3), 152–162. ISSN 0213-6163. Available at: doi:10.1016/j.ejpsy.2021.11.002

Document Type: Review; IF = 1,800; median IF PSYCHIATRY – SSCI 3,000; according to IF PSYCHIATRY Q4; according to AIS PSYCHIATRY – SSCI Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	45	40	50

[12]**BREZNOSCAKOVA, Dagmar** and Maria PALLAYOVA. Uncovering the Untold Emotional Toll of Living with Diabetes in the COVID-19 Era. *Psychotherapy and Psychosomatics* [online]. 2022, **91**(4), 286–287. ISSN 1423-0348. Available at: doi:10.1159/000524178

Document Type: Letter; IF = 22,300; median IF PSYCHIATRY – SCIE 3,700; PSYCHIATRY Q1; according to AIS PSYCHIATRY – SCIE Q1, 4th most prestigious journal in the world in the psychiatry category, 3rd most prestigious in the psychology category

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	45	40	50

[13]**IZAKOVA, Lubomira, Dagmar BREZNOSCAKOVA, Katarina JANDOVA, Vanda VALKUCAKOVA, Gabriela BEZAKOVA and Jozef SUVADA**. What mental health experts in Slovakia are learning from COVID-19 pandemic? *Indian Journal of Psychiatry* [online]. 2020, **62**(Suppl. 3), S459–S466. ISSN 1998-3794. Available at: doi:10.4103/psychiatry.IndianJPsychiatry_758_20

Document Type: Article; IF = 1,759; median IF PSYCHIATRY – SCIE 3,429; according to IF PSYCHIATRY Q4; according to AIS PSYCHIATRY – SCIE Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	35	30	35