

STATEMENT OF OPINION
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ABOUT: Regarding the dissertation for the award of the educational and scientific degree "Doctor" (PhD)

Field of Higher Education: 7. Healthcare and Sports

Professional Field: 7.1. Medicine

Scientific Specialty: Pathophysiology

Author of the dissertation: Dr. Gabriela Georgieva Panayotova, full-time PhD student at the Department of Physiology and Pathophysiology, Medical University – Varna.

Dissertation Title: "EVALUATION OF THE POTENTIAL THERAPEUTIC BENEFITS OF BIOFEEDBACK TRAINING AS A METHOD FOR REDUCING STRESS AND IMPROVING THE MENTAL HEALTH OF INTERNATIONAL MEDICAL STUDENTS"

Scientific Supervisor:

Prof. Margarita Stefanova Velikova, MD, PhD

By Order No. R-109-283/30.07.2026 of the Rector of MU-Varna, I was appointed as a member of the scientific jury for the dissertation defense procedure of Dr. Gabriela Georgieva Panayotova, and by the decision of the jury's first meeting (Protocol No. 1/11.08.2026), I was assigned to submit a Statement opinoin on the procedure.

Overview of the Procedure

All reviewed documents presented for the application in the competition are in accordance with the requirements of the Act on Development of the Academic Staff in Republic of Bulgaria, the Rules for its implementation and the Regulation for holding the academic position, adopted by the Rules for Academic achievement in Science of the Medical University of Varna.

The dissertation submitted for review comprises 185 pages; it is structured into 11 chapters and illustrated with 40 figures, 30 tables, and 7 appendices. The bibliography comprises a total of 645 sources in Latin script. The abstract consists of 111 pages, 28 figures, and 28 tables. Both the dissertation and the abstract are well-structured, maintaining an optimal balance between sections appropriate to the topic, and include all essential elements: introduction, literature review, aim and objectives, materials and methods, results, discussion, conclusion, findings, scientific contributions, practical recommendations, a list of publications and scientific communications related to the work, and the bibliography. Reading the dissertation leaves the

impression of a concise and competent presentation of the research, demonstrating in-depth knowledge, a creative approach, and critical analysis regarding both the subject matter and the cited literature. The dissertation is written in good Bulgarian, characterized by clear sentences and precise reasoning. In this study, the doctoral candidate, Dr. Gabriela Panayotova, and her supervisor present a comprehensive approach to assessing stress factors among international medical students, while simultaneously evaluating the efficacy of biofeedback training as a potential therapeutic method for reducing stress and improving their mental health.

Candidate's CV and career profile

Dr. Gabriela Georgieva Panayotova was born on April 14, 1995, in the town of Gorna Oryahovitsa. In 2020, she graduated with honors and numerous awards from the Medical University of Varna, specializing in Medicine. Since 2021, she has served as a full-time Assistant Professor, and since 2023, as a full-time PhD candidate in the Physiology Unit of the Department of Physiology and Pathophysiology at the Medical University of Varna. Between 2020 and 2025, she acquired additional specializations and qualifications, including: a Master's degree in Artificial Intelligence in Biomedicine; a Master's degree in Health Management and Medico-Social Care; the Global Clinical Scholars Research Training program at Harvard Medical School (Boston, USA); and a specialization in Physiology. During her clinical medical training, Dr. Gabriela Panayotova completed numerous internships both in Bulgaria and abroad, including at: the Department of Pediatric Surgery at St. Anna University Hospital, Varna; the Department of General Surgery and Gastroenterology at Pomeranian Medical University, Szczecin, Poland; the Department of Anesthesiology and Intensive Care at North-Western State Medical University named after I.I. Mechnikov, St. Petersburg, Russia; and the Department of Pediatrics at the Faculty of Medicine, Rey Juan Carlos University, Madrid, Spain.

Significance of the Issue

The selected subject holds considerable relevance and importance from both theoretical and clinical viewpoints, particularly due to the escalating incidence of anxiety-depressive illnesses and the emergence of enduring functional and organic impairments resulting from chronic stressors in contemporary society. Stress serves as a significant risk element for the onset of many illnesses and a crucial marker of a person's physiological condition. In the 1920s and 1930s, the notion progressively infiltrated biological and psychological writings, where it was employed to denote mental stress or detrimental environmental influences that could incite illness. Modern interpretations of the concept utilise Selye's broadened perspective on stress as a universal adaptive mechanism that encompasses both physiological and psychological processes; in this context, "eustress" refers to the beneficial effects of moderate stress, while "distress" pertains to negative physiological and psychological outcomes. In contemporary literature, "stress" includes a wide spectrum of experiences—from slight annoyance to severe problems that may result in considerable health decline. In everyday language, nearly any occurrence or circumstance—irrespective of its severity or any ramifications—can be characterised as stressful.

On an international level, the pressures impacting university students are inadequately researched. A primary obstacle is discerning the processes that connect chronic stress—be it metabolic, social, or physical—to cardiovascular ailments and immune system impairment. The incidence of chronic stress is notably elevated among medical students, particularly those pursuing studies overseas, owing to rigorous academic demands, cultural disparities, the necessity to acclimatise to a novel setting, the lack of familial and social support, and possible financial challenges. These pressures can significantly affect psychological well-being and academic achievement, resulting in burnout along with both physical and mental fatigue. It is essential to investigate the correlation between stress, which acts as a catalyst for anxiety and depressive disorders, and its immediate physiological impacts, while also considering preventive measures to avert difficulties.

Biofeedback (BF) has recently attracted heightened attention as a supplementary stress management technique for diverse groups and as an adjuvant to traditional therapies for anxiety disorders and depression. BF facilitates the instantaneous observation of physiological metrics—like heart rate, muscle tension, and brainwave patterns—in persons under stress; concurrently, through training and targeted methods, participants can cultivate the capacity to consciously regulate these variables.

The therapeutic efficacy of BF in alleviating stress among international medical students has not been adequately researched. Contemporary research predominantly emphasises students in their native countries or clinical groups, resulting in a deficiency in comprehending the distinct requirements and responses of international students, who encounter unique obstacles—such as linguistic hurdles and social seclusion—that influence their stress levels. This research presents an all-encompassing methodology for measuring stressors faced by international students, concurrently examining the effectiveness of biofeedback (BF) training as a possible therapeutic intervention for alleviating stress and enhancing mental well-being. A crucial element is the advantageous safety characteristics of biofeedback: the technique is non-invasive, necessitates active involvement from participants, and allows individuals to employ self-regulation abilities to manage and alleviate stress, therefore enhancing mental well-being relative to traditional treatments.

The outstanding concerns underscore the importance of the subject chosen by the doctoral candidate and their advisor, prompting me to determine that the dissertation topic is both meaningful and appropriate for a doctoral thesis.

In the introduction, Dr. Panayotova has effectively articulated a succinct summary of the scientific dimensions of the issue, the objectives of the research, and its significance to the discipline.

The literature review delineates and elucidates modern facets concerning the characterisation of acute and chronic stress and the stress response system, alongside the explored pathogenetic connections among stress, somatic illnesses, depression, and anxiety disorders. The presentation exhibits a proficient and analytical examination of data pertinent to the discipline. The impact of prolonged stress on the hypothalamic-pituitary-adrenal axis, the central nervous system (CNS), and the immune system—alongside the pathophysiological processes that result

in dysfunction and depressed behavior—are analysed in a coherent and methodical fashion. The PhD candidate has thoroughly examined the effects of stress on the cardiovascular, pulmonary, gastrointestinal, musculoskeletal, immunological, and reproductive systems. Particular emphasis is placed on the immune system's function in safeguarding the body from infections during stressful circumstances. The focus is on structural alterations in the central nervous system linked to the impact of the stress system in relation to depression and anxiety disorders.

The frequency and primary contributors to stress experienced by overseas students are thoroughly outlined, along with the potential factors linked to the onset of anxiety and depression in this demographic. The PhD candidate examines experimental methodologies employed worldwide—encompassing both human and animal participants—to investigate diverse stressors pertinent to the advancement of the biofeedback (BF) technique and its therapeutic uses, such as mental health, pain alleviation, cardiovascular wellness, and urinary and faecal incontinence. Dr. Gabriela Panayotova has a profound understanding of the fundamental issue, alongside a methodical perspective and proficiency in choosing suitable research methodologies informed by the referenced literature. The principal elements of the dissertation and the working hypothesis are articulated and examined with considerable proficiency, aiding the reader's progression to the resultant aim and objectives, which are rationally justified.

Aim and Objectives:

The aim is clearly and precisely formulated and accurately reflects the author's intentions. The doctoral candidate aims to evaluate the therapeutic potential of biofeedback (BF) training as a method for reducing stress and improving the mental health of international medical students.

To achieve this scientific aim, five key objectives have been set, involving the sequential application of various methodological approaches to assess levels of stress, anxiety, and depression among international medical students through the administration of highly informative and validated psychometric tests:

1. Perceived Stress Scale (PSS);
2. Anxiety (Zung Self-Rating Anxiety Scale [SAS] and Beck Anxiety Inventory [BAI]);
3. Depression (Beck Depression Inventory [BDI]).

The objectives are formulated clearly and specifically; they align with the stated aim and follow the working hypotheses.

Materials and Methods:

The study setup and design—incorporating various tests and methods for assessing stress across different situations and conditions—are presented with great competence. In this regard, the doctoral candidate demonstrates excellent theoretical and practical preparation. I highly value the personal effort and contribution the candidate has invested in mastering and applying

the described labor-intensive methods and techniques, including the accurately detailed statistical analyses. The volume of research material is fully adequate, and the diverse methods and approaches employed—along with statistical processing—enable the generation of scientifically grounded, comparable results while minimizing deviations and inaccuracies. The choice of methodology aligns with the nature of the data, the hypotheses, and the study design, which incorporates repeated measurements over time, a control group, and a wide range of physiological and psychometric indicators. Descriptive, comparative, variance, longitudinal, multivariate, factor, correlation, and regression analyses were conducted, combining descriptive, comparative, longitudinal, and multidimensional approaches to ensure a valid interpretation of the therapeutic effects of BF training on the participants' mental and physiological states. All tests were considered statistically significant at a significance level of $p \leq 0.05$.

Results

Despite their substantial volume, the obtained results are described concisely and clearly illustrated with figures and tables. The distribution of the studied students according to group, gender, age, and stress levels is examined systematically, in alignment with the dissertation's stated aim and objectives. I highly value all the presented data as innovative and significant for characterizing the etiopathogenesis of psychological distress and the resulting pathological processes—anxiety, depressive symptoms, changes in serum IgA levels, and cortisol reactivity—as well as the impact of biofeedback training on these factors in international medical students.

In the discussion of the results, the doctoral candidate has adopted a critical approach, analyzing both their own findings and data from the cited literature. The discussion is closely linked to the aim, objectives, and hypotheses formulated in the literature review. The doctoral candidate demonstrates a profound understanding of the issue and an analytical approach to handling data, facts, and interpretations. This confirms the author's ability to synthesize and analyze information.

The nine conclusions reached are accurately articulated and logically derived from the specified aim and objectives. The findings and inferences of the study yield rational contributions, which are detailed in the contributions section.

This work comprises 11 contributions: 7 that are original and 4 that are confirmatory.

Original Contributions:

1. For the first time, a controlled longitudinal study of the effect of HRV-based biofeedback training in international medical students was conducted, combining psychological, autonomic, and biochemical indicators of the stress response.
2. A model for psychophysiological monitoring of the individual response to biofeedback training was developed, in which data from psychometric measurements are analyzed jointly with heart rate variability indicators and salivary cortisol and IgA.

3. A structured HRV-based biofeedback training protocol was developed (an 11-week program conducted in real time, including controlled breathing, attentional focusing, and visual feedback).
4. Comparative modeling of the predictive value of HRV, salivary cortisol, and secretory IgA with respect to changes in psychophysiological state was performed, revealing the greater informativeness of baseline HRV profile indicators regarding improvement in perceived stress and anxiety.
5. A multisession approach was applied to assess autonomic regulation during the biofeedback program, enabling HRV to be monitored as individual dynamics across successive training sessions.
6. A methodological foundation was established for future multidisciplinary studies of stress and self-regulation, integrating psychometric assessment, HRV analysis, and measurement of hormonal and immunological indicators.
7. A basis was established for developing digital formats for remote monitoring and support of self-regulation through HRV-based biofeedback technologies aimed at monitoring and preventing academic stress.

Confirmatory Contributions:

1. The results support the evidence for a favorable effect of an HRV biofeedback training program on perceived stress, anxiety, and depressive symptoms in young people and student populations.
2. The understanding of the informativeness of different physiological indicators in monitoring the effect of BF training was expanded. The more pronounced dynamics of the psychometric indicators are consistent with evidence that psycho-emotional improvement after biofeedback occurs more rapidly and significantly than changes in autonomic and biochemical markers.
3. The comprehensive approach applied emphasizes the importance of combined assessment using psychometric instruments, HRV indicators, and biochemical markers, because each reflects a different aspect of the psychophysiological response to stress and intervention.
4. The absence of a specific effect of the biofeedback program on salivary cortisol and IgA is consistent with evidence of the high individual and contextual variability of these markers, which limits their use as independent indicators of short-term psycho-emotional improvement.

The candidate's scholarly contributions pertinent to the dissertation subject include three articles in peer-reviewed journals, thereby satisfying the criteria for the defence. The PhD applicant has showcased the findings of their dissertation at four global scientific conferences.

Suggestions and observations

I possess no substantial critiques concerning the final iteration of the dissertation or the accompanying material. Dr. Gabriela Georgieva Panayotova's dissertation offers both scientific

and practical value, indicating that the candidate should prioritise the dissemination of the acquired findings in the future.

Final assessment

The dissertation authored by Dr. Gabriela Georgieva Panayotova, entitled "**Evaluation of the potential therapeutic benefits of biofeedback training as a method for reducing stress and improving the mental health of international medical students**" offers both theoretical and practical findings that represent a novel addition to the discipline and fulfill the stipulations of the *Act on the Development of the Academic Staff in the Republic of Bulgaria* for the awarding of the educational and scientific title of "Doctor" (PhD).

In view of the above, my overall assessment of the submitted dissertation—"Evaluation of the potential therapeutic benefits of biofeedback training as a method for reducing stress and improving the mental health of international medical students"—is POSITIVE. Accordingly, I unreservedly recommend that the esteemed members of the Scientific Jury vote in favor of awarding the educational and scientific degree of "Doctor" (PhD) in the doctoral program of "Pathophysiology" to Dr. Gabriela Georgieva Panayotova.

20.09.2026

Varna

Assoc. Prof. Kameliya Bratoeva, MD, PhD

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