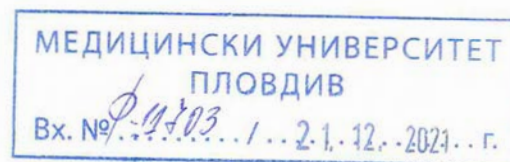


To the Chairman of the Scientific Jury,  
Appointed by Order № P - 1882 / 22.10.2021  
of the Rector of the Medical University of Plovdiv

On your Protocol №1/ 03.11.2021.



**Attached I present: Opinion**

in a competition for the academic position of "Associate Professor".

in the scientific specialty "Psychiatry".

announced for the needs of MU-Plovdiv, department Psychiatry and Medical Psychology.

in State gazette, no. 63 / 30.07.2021

**Reviewer:** Full Professor Olga Dmytrivna Lytvynenko, Dr. of Science  
Scientific specialty/ies Psychology  
Institution: Odessa National I.I. Mechnikov University, Ukraine.

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*The opinion has been prepared under the requirements of the Law on the development of the academic staff in the Republic of Bulgaria and Section III / Section IV of the Rules for the application of the Law on the development of the academic staff in the Republic of Bulgaria and procedure for holding the academic position of "Associate Professor".*

OPINION  
OF PROF. OLGA DMYTRIVNA LYTVYNENKO, DR. OF SCIENCE  
FOR THE COMPETITION FOR OCCUPATIONAL ACADEMIC POSITION  
"ASSOCIATE PROFESSOR"  
IN MU-PLOVDIV

Member of the scientific jury appointed by Order № P1882 / 22.10.2021 of the Rector of the Medical University - Plovdiv for conducting a competition for the academic position of "Associate Professor" for the needs of the Medical University - Plovdiv, Department of Psychiatry and Medical Psychology for teaching Bulgarian and English in the scientific specialty "Psychiatry" professional field 7.1 "Medicine", a field of university education 7. "Health and Sports", announced in SG no. 63 of 30.07.2021

*APPLICANT: Dr. Sevdalina Sevdalinova Karaivanova-Kandilarova, Ph.D. – chief assistant at the Department of Psychiatry and Medical Psychology, Medical University of Plovdiv.*

**I. Analysis of the applicant's career profile.**

Dr. Kandilarova graduated with a master's degree in medicine from MU - Plovdiv with excellent results in 2005. In the period August 2006 - May 2007 she was an assistant researcher in the Research Group at fMRI (functional magnetic resonance imaging) in the Department of Cognitive Neuroscience, Department of Biological and Medical Psychology at the University of Bergen, Norway under the direction of Prof. Kenneth Hugdal. From October 2007 to September 2008 she worked as a resident doctor in the Department of Gerontopsychiatry at the Psychosomatic Clinic of the University Hospital Haukeland, Bergen, Norway. Subsequently (from 2008 to 2010) she specialized in Psychiatry at the Tertnes Psychiatric Clinic at the Haukeland University Hospital, Bergen, Norway.

In 2012, she returned to Bulgaria and was enrolled as a full-time doctoral student at the Department of Psychiatry and Medical Psychology, MU-Plovdiv. The topic of her dissertation is "Neurophysiological markers for diagnosis and prognosis in depression". In 2013 she continued her specialization in the Clinic of Psychiatry and Medical Psychology of the University Hospital "St. George" Plc., Plovdiv, which ended successfully in 2017 with a degree in Psychiatry. In February 2014 she was selected as an assistant professor of English at the Department of Psychiatry and Medical Psychology, Medical University of Plovdiv.

For more than 5 years (October 2015-January 2021) she was a member of the team in the field of "Psychiatry" at the Research Complex of Translational Neuroscience at MU-Plovdiv, where her main activities were related to the design and programming of paradigms for fMRI, extraction, and analysis of data from fMRI. In the period 2013-2018, she participated in several training courses (Bergen, Norway; Basel, Switzerland) related to the application of neuroimaging methods to study the structure and function of the human brain. She has won twice individual mobility grants under a program of the European Economic Area Scholarship Fund.

In 2017, Dr. Kandilarova obtained the educational and scientific degree "Doctor" after successfully defending her dissertation to a scientific jury, including researchers from global

(American and European) centers for neuroimaging. Since March 2018, after a successful competition, she has been appointed as an Assistant Professor in the same department.

In February 2021 she was appointed as a specialist in psychiatry at the Clinic of Psychiatry, and Medical Psychology of the University Hospital "St. George" Plc., Plovdiv, where she continues to work up to now.

Dr. Kandilarova is fluent in English and has a good knowledge of French and Norwegian.

Overall assessment: Dr. Sevdalina Kandilarova began her career development at the University of Bergen, Norway, where she worked with internationally recognized experts in the field of psychiatry and cognitive neuroscience. Then she began a specialization in Psychiatry at the University Hospital in Bergen. Returning to Bulgaria, she developed her professional and research qualities in the Clinic of Psychiatry, the Department of Psychiatry, and Medical Psychology and the Research Complex in Translational Neuroscience. In this academic community with established traditions, she continues and expands her contacts with experts in the field of neuroimaging from Norway and Switzerland, thanks to which she acquires in-depth theoretical knowledge and practical skills. The collaboration with European centers with high expertise in the field of neuroscience and Dr. Kandilarova's perseverance leads to her development as a highly qualified specialist and researcher.

## II. General description of the materials submitted in the competition.

The materials submitted by Dr. Kandilarova are in full and comply with the requirements of LDASRB and the Regulations of MU - Plovdiv. The necessary evidence for career development (professional and academic - with the relevant diplomas, documents, references, and certificates), as well as for teaching and research activities (academic reports on workload, list, and copies of publications, as well as summaries in Bulgarian and English), list of textbooks, citations, and participation in projects with evidence). The evidence is comprehensive and corresponds to the list published on the website of MU - Plovdiv.

Dr. Kandilarova participates in the competition with 29 scientific papers, 20 of which are full-text publications in foreign journals with impact factor (mainly between 3 and 5, maximum IF 9.306), 2 - in foreign refereed journals without impact factor, also 2 in national journals and scientific journals, 3 are abstracts in foreign journals with impact factor, 1 abstract is in foreign journals/collections without impact factor and 1 abstract of participation in a national forum.

The applicant participates in the author's team of 4 textbooks in Psychiatry for medical students in Bulgarian and English and in Medical Psychology for medical students in Bulgarian and English. She assists in the preparation of tests and teaching materials before and during the online training for which she is responsible in the department.

Dr. Kandilarova presented in the competition a total of 50 citations of her scientific papers. All of them are in refereed journals and 49 of them are in publications with IF mostly between 3 and 6. the maximum IF is 13,382.

Evidence was provided of the applicant's participation in 2 international projects, 3 national projects (one of which with international participation), and 4 intra-university projects.

### III. Assessment of the applicant's scientific works for the overall academic development.

✓ General characteristics of the scientific production and publishing activity:

Dr. Kandilarova participates in the competition with 24 full-text scientific publications, 4 textbooks, and 5 scientific reports. The scientific publications (24) include 20 actual publications in scientific journals with impact factor, 2 in refereed journals without IF, and 2 in non-indexed national journals without IF. It is noteworthy that most of the publications are in magazines with IF. The candidate is the first or second author in 15 of all publications. Most own original studies are presented and only 4 of the articles are reviews. The applicant has co-authored with researchers from abroad.

Dr. Kandilarova's scientific production and publication activity are grouped in the following areas:

#### *Unconventional functional MRI*

In continuation of the applicant's doctoral dissertation, an upgrading paradigm has been developed, which has been applied to patients with schizophrenia and depression, and the results have been reported in most of the presented publications (over 10). The doctoral dissertation data presented the sensitivity of the method of translational cross-validation of clinicopsychological scales and fMRI (its ability to distinguish norm from pathology), on the other hand, the post-doctoral thesis expressed that there is evidence for its specificity - an ability to distinguish individual mental disorders. An innovative method was used to analyze multimodal data from structural and functional imaging during rest and when performing tasks through multivariate analysis based on machine learning. Convincing data have been generated for successful convergent cross-validation between clinico-psychological assessment scales and fMRI images. Specific activations and brain signatures specific to different patients' groups (with the paranoid and depressive syndrome) have been found. The contribution of the various modalities (structure, function during the rest, and function during the performance of a task) to the differential diagnosis of schizophrenia and affective disorders has a particularly high scientific and applied value. The applicant's overall work in this field significantly contributes to the development of methods of translational neuroscience and their application in Psychiatry.

#### *Conventional functional MRI when performing tasks*

The applicant has developed and implemented an original block paradigm for the simultaneous application of visual stimuli from the International Affective Pictures System (IAPS) and fMRI with patients with depression and healthy controls. Significant theoretical and methodological contributions in this field are the evidence found for the advantage of the methods of multivariate analysis in multimodal data from structural and functional magnetic resonance imaging during a task, compared to widely used classical univariate methods.

#### *Functional MRI during a rest*

Dr. Kandilarova also presents several studies on brain connectivity measured by fMRI during a rest. A comparison between patients with depression and healthy controls using the method of spectral dynamic causal modeling revealed disorders in the functional connections between different nodes of the brain network. The results emphasize the role of the anterior insula in the pathophysiological mechanisms of depression and find a wide response in the literature (for 2 years over 20 citations in journals with IF up to 13,382).

In a transdiagnostic study of patients with schizophrenia, bipolar and monopolar depression, potential differential diagnostic markers have been found with an overall accuracy

of up to 75%, which is a significant contribution to the detection of connectivity disorders in major mental disorders.

#### *Structural MRI*

Data on structural disorders in depressed patients compared with healthy controls have been published. The quantitative method of voxel-based morphometry has been used and it has been found that depression is associated with a significant reduction in the volume of gray matter in certain regions located in the frontal and temporal lobes. A significant contribution is a subsequent meta-analysis, in which comparison has been made between depression, anxiety disorders, and post-traumatic stress disorder, which identified structure-specific structural correlates.

- ✓ Scientific activity - dissemination and application of applicant's scientific and practical achievements within the scientific community;

Dr. Kandilarova actively participates with reports at international and national conferences and three of the announcements have been published in journals with IF. The main applicant's applied-practical contribution is the developed original paradigms for fMRI during performing tasks.

- ✓ Participation in project implementation:

Dr. Kandilarova participated in 2 international projects, respectively with the University of Bergen Norway and the University of Lausanne, Switzerland. The first project focused on the study of hallucinations by fMRI during rest and led to several joint publications. The second project aimed to test an innovative platform for the automatic analysis of MRI data.

The applicant also participated in 3 national projects, one of which with international participation, as well as in 4 intra-university projects where she collaborated with researchers from the departments of Microbiology and Immunology, Pathological Physiology, Biology.

- ✓ Scientific and creative achievements (scientific authority);

Dr. Kandilarova has received well-deserved recognition for her scientific achievements, as evidenced by the high citation index (Hirsch Index 7 in Scopus). She is a reviewer of prestigious impact magazines such as the Journal of Affective Disorders and Acta Radiologica and has produced 8 reviews for various national and foreign journals.

#### **IV. Evaluation of the monographic work or equivalent publications submitted for participation in the competition for "ASSOCIATE PROFESSOR".**

10 original publications in refereed editions with IF are presented, which can be combined in the following areas of interest.

#### *fMRI during rest*

Dr. Kandilarova focuses on extremely current research on brain connectivity during rest using the method of **effective connectivity**. With its help, not only the connection between the regions of interest is determined, but also the direction and strength. The results make it possible to determine the respective inhibitory or excitatory effect of one region on another. In a study of individuals with depression and healthy controls, patients have been found to have significantly reduced strength of

the connection from the anterior insula to the dorsolateral prefrontal cortex and demonstrated a link between the amygdala and the anterior insula that is missing in the healthy controls. In addition, a significant correlation has been found between the severity of depression and the connectivity of the hippocampal node.

A similar study was performed with patients with schizophrenia and those with depression, combining data from fMRI during rest and in the implementation of an unconventional paradigm for translational validation of clinical psychological scales. The study has found an aberrant relationship between the anterior insula and the medial frontal gyrus, showing a significant difference between the two groups with an inhibitory relationship found only in patients with schizophrenia.

The findings of both studies could suggest that the association between the dorsolateral prefrontal cortex (DLPFC) and the anterior insula can be interpreted as evidence of an aberrant network that leads to behavioral abnormalities that depend on the direction of impact. Decreased effective connectivity from anterior insula to DLPFC manifests as depressive symptoms, and the inhibitory effect of DLPFC to anterior insula is reflected in the paranoid symptoms of schizophrenia. These conclusions represent a significant contribution to the hypotheses of disconnectivity as a major pathophysiological mechanism in psychotic and affective disorders.

#### *Structural MPI at depression*

A study has been reported using the quantitative method of voxel-based morphometry applied to patients with depression (50) and healthy controls (42). Depression is characterized by a significant reduction in the volume of gray matter in certain regions located in the frontal and temporal lobes. The results have been subsequently used in a meta-analysis comparing patients with depression, anxiety disorders, and post-traumatic stress disorder. Structural correlates specific to individual disorders have been found, which enriches our understanding of the neurobiological mechanisms of these common mental disorders.

#### *Unconventional fMRI during performing a task – classical univariants and multivariate analyzes*

The applicant has participated in the development of an innovative research model that combines routinely used scales for clinical psychological (psychiatric) assessment with the simultaneous use of functional magnetic resonance imaging (MRI). The aim is to find "bridges" of translation between neuroimaging markers and clinical psychological scales, which will objectify an otherwise relatively subjective assessment based on what is shared by the patient. The successful application of this method in patients with depression and healthy controls is the basis of her doctoral dissertation, which proves the sensitivity of the method (its ability to distinguish normal from pathology). As part of this project, an upgrading paradigm has been developed that has been applied to patients with schizophrenia and depression (in the context of bipolar or major depressive disorder). The results of this study, reflected in five of the presented publications, prove the specificity of the method, i.e. the ability to distinguish between different psychopathological constructs.

Along with the classical univariate analyzes, two publications have also used a multivariate analysis based on machine learning using multimodal data from structural and functional imaging during rest and when performing tasks. Due to this, convincing data have been generated for the successful convergent cross-validation between clinico-psychological scales for evaluation and fMRI images with the establishment of specific activations and brain signatures specific to different groups of patients (paranoid and depressive syndrome). The contribution of the various modalities (structure, function at rest, and function in the performance of a task) to the differential diagnosis of schizophrenia and affective disorders has a particularly high scientific and applied value.

### *Conventional functional MRI during performing tasks*

The applicant's contribution is the developed original block paradigm for fMRI with visual stimuli from the International Affective Pictures System (IAPS), which is applied to patients with depression and healthy controls. The main theoretical and methodological contributions in this field are the evidence found for the advantage of the methods of multivariate analysis in multimodal data from structural and functional magnetic resonance imaging in the task, compared to widely used classical univariate methods.

**V. Reflection (citation) of the candidate's publications in the national and foreign literature (publication image).**

Proof of the qualities of Dr. Kandilarova's scientific publications is their high international evaluation, reflected in the presented positive citations, which are a total of 50. It is noteworthy that 49 of them are in journals with impact factor, mostly between 3 and 6. The publication establishing impaired effective connectivity of the anterior insula in depression is cited in an article in a publication with a very high IF - 13,382. The applicant's Hirsch index is 7 according to a check at the Scopus database.

**VI. Comprehensive, quality assessment of teaching and teaching activities, including scientific guidance of students, doctoral students, postgraduates.**

Dr. Kandilarova has over seven years of teaching experience as an assistant at the Department of Psychiatry and Medical Psychology at MU-Plovdiv. She has been actively involved in the practical training of students in medicine and dentistry since 2014. In the period 2015-2017, she had lectures and practical exercises in a course in gerontopsychiatry for students from the Medical College, specialty "Nurse" and "Midwife". Throughout her teaching career, she has conducted practical exercises for students of medicine and dentistry in English and participates in Erasmus training. Since 2016 she has been contributing to the training of general practitioners. Since 2017, she has systematically trained students, Ph.D. students, and lecturers in the methods for paradigm design and data processing by fMRI. In 2020 she organized and conducted specialized theoretical and practical training for students and doctoral students in the methods of fMI. According to the academic report for the last 3 academic years, the study load of Dr. Kandilarova is much above the norm (on average over 200%).

Proof of Dr. Kandilarova's activity in the transfer of experience to potential future researchers is the attached list of over 15 publications and projects with students and Ph.D. students' participation.

**VII. Critical remarks and recommendations.**

None.

**VIII. A general assessment of the applicant's compliance with the minimum national requirements under Article 2b, paragraph 2 and 3, respectively to the requirements under Article 2b, paragraph 5 of LDASRB and the specific requirements of MU - Plovdiv in areas**

and for units with/without clinical activity, defined in the Regulations for academic development at the Medical University – Plovdiv

As it can be seen from the attached table, the applicant's performance is several times higher than the minimum requirements.

Group of indicators	Minimum requirements	Real applicant's indicators
Group A	50	50
Group B	100	103.37
Group C	200	244.14
Group D	100	750
Group E	60	196.7
Group F	300	677.25
<b>Total</b>	<b>810</b>	<b>2021.46</b>

**IX. Conclusion:**

*The applicant fully meets the mandatory and specific conditions and scientometric criteria for holding the academic position "ASSOCIATE PROFESSOR". Based on this, I give a positive opinion for the award of the academic position of "Associate Professor", in the scientific specialty Psychiatry, in the Department of Psychiatry and Medical Psychology at MU - Plovdiv to Dr. Sevdalina Sevdalinova Karaivanova-Kandilarova, Ph.D.*

15. 12. 2021

Odessa, Ukraine

Opinion prepared by:

Professor Olga Dmytrivna Lytvynenko,

Dr. of Science

