

Attitude of Reviewer

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Re: defense of dissertation for acquisition of scientific degree "Doctor of Science" the Professional field 4.3. Biological Sciences, specialty "Anthropology" in the Department "Anthropology and Anatomy" of IEMPAM-BAS

Author: Assoc. Prof. Silvia Nikolova, PhD in IEMPAM-BAS

Title: Biomedical aspects of cranial sutures: microstructure, physiological closure, metopism

Brief presentation of the author and the dissertation work

Associate Professor Silvia Nikolova, PhD, graduated from the Faculty of Biology of the University of St. Kliment Ohridski" in 2003 with a master's degree in general anthropology. She started her carrier in IEMPAM-BAS as a PhD student and defended her PhD thesis in 2010 on the topic "Anatomical variations of the skull - anthropological characterization and assessment of gender and bilateral differences". In 2011 Dr. Nikolova held the academic position "Assistant", in 2012 she was promoted into Assistant professor, and in 2023 she acquired academic position Associate professor in the specialty of anthropology".

Assoc. Prof. Nikolova presented a set of materials on a CD including a dissertation, a summary project and all the required documents according to the Regulations of IEMPAM for the acquisition of scientific degrees and for holding academic positions. The dissertation is written on 251 pages in a balanced ratio between the individual sections with a characteristic predominance of "Results and discussion" section - 134 pages. The results are illustrated with 28 tables and 71 figures, 18 of which are diagrams and graphs, and the remaining 53 figures are cranial images. The reference list includes 378 sources from the scientific literature in English. Appendix explains terms, indices, parameters, measurements, anatomical variations, etc.

Timeliness and current state of research on the problem

The doctoral dissertation by Assoc. Prof. Nikolova deals with questions of fundamental importance related to the formation, functioning and closure of cranial vault sutures. The physiological key importance of these processes for normal morphogenesis of the skull determine the timeliness of the dissertation work. Its importance for obtaining new knowledge is understood by the interdisciplinarity of the dissertation work using artificial intelligence approaches to find the answers to a number of questions about metopism. For example there is lack of one/unified hypothesis about what imposes the programmed, early closure of the metopic suture, on the one hand, and on the other hand, it is not clear what causes the suppression of this programmed physiological closure and what are the factors regulating this process.

The high competence of the author is evident from the literature review, written on 40 pages, which makes a detailed and critical presentation in a compact form of the data published so far. The literature review ends with a short annotation summarizing the unresolved issues in the research topic. The author motivates her scientific interest in metopism by the fact that, due to the key role of sutures in the morphogenesis of the skull, any deviation from the usual terms of their formation, functioning and closure has an impact on cranial morphology. This requires metopism to be considered as a complex state, i.e. as a consequence/expression of a developmental disturbance rather than a prerequisite for differences in cranial morphology. In this aspect, the author motivates why need to conduct complex and comparative studies in homogeneous and statistically representative metopic and control cranial series for the purpose of her work.

Aim, tasks and methodological approaches of the dissertation

The dissertation aims to study the microstructure and physiological closure of the cranial sutures and to evaluate the specifics in the cranial morphology in metopism. This means investigating the bone microarchitecture, by means of three-dimensional imaging, applying interdisciplinary approaches to data analysis and interpretation. In order to achieve the goal, six tasks have been formulated in a short and concise form. Extensive material from the ossuary of the National Military History Museum - Sofia and cranial series from the IEMPAM osteological collection were used in an amount guaranteeing reliable results. The material is processed with non-destructive methods, including classical, modern and innovative techniques. The material has been digitized by means of digital radiography, the generation of volumetric three-dimensional images and of polygonal three-dimensional models. The collected data were processed using digital morphometry. They have been analyzed by applying classical and modern statistical methods, geometric morphometrics and the methods of artificial intelligence (machine learning and data mining). The use of a significant number of software (13 pieces) is impressive.

Results and discussion

The section is presented in 6 chapters on 134 pages. Characteristic of the complexity of "Doctor of Sciences" theses, the results in the present work are presented together with the discussion and self-assessment of their originality and innovation. The foundation for studying cranial suture closure is based on an original descriptive scale developed by the author to measure the degree of suture closure, which allows her to hypothesize that the factors keeping the metopic suture open do not act in isolation in the frontal region. For the first time, a model has been developed to determine age at death by sagittal suture closure, and although it is not indicative for forensic purposes, it can be applicable in osteological examinations. Comparative analyzes between metopic and non-metopic series showed that metopic skulls were characterized by specific modifications in the morphology of the cranial vault, orbital and naso-frontal regions, but showed no significant difference in the profiling of the skull base. Original data were obtained that the persistent metopic suture is accompanied by reduced pneumatization of the frontal sinus, which is a spatially coordinated process in the vertical and horizontal part of the frontal bone. Metopism is often accompanied by the formation of supernumerary bones in the cranial vault, formed by fragmentation of the normal ossification centers, as well as by the formation of additional centers in the cranial sutures and fontanelles. That is why Dr Nikolova considers metopism as a

generalized disturbance in intramembranous ossification, which is overexpressed in some types of skeletal dysplasia.

Conclusions and achievements

The section "Results and Discussion" ends with "Summary", which represents the essence of the contribution and innovative potential of the dissertation work. Six conclusions have been formulated that correspond to the 6 tasks set. Six fundamental/theoretical and 6 applied achievements were formulated. The fundamental achievements correspond to the conclusions of the dissertation. The applied achievements demonstrate the innovativeness of the methodical approaches used - an original method for scanning objects larger than the micro computer tomography system; 4-level scale for evaluating the degree of sagittal suture closure; constructing point configurations describing the morphology of the whole skull and its parts; adapting methods from the field of artificial intelligence. Last but not least is the creation of a virtual collection of three-dimensional images, which is a unique base for the study of metopism.

I would like to point out that Dr Nikolova revised the text following my recommendations during the discussion of the dissertation work.

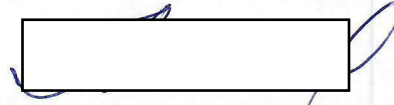
Publication activity and quality of scientific production

Assoc. Prof. Nikolva presented a list of 32 publications related to the topic of the dissertation, 30 of which were published in journals indexed in Web of Science and Scopus (19 with impact factor and impact rank), which demonstrates the high quality of her scientific output. According to indicator D, Assoc. Nikolova has 120 points, presenting 5 articles with quartiles (4 with Q1 and 1 with Q2), which were not used for registration in NACID during previous academic promotion procedures. According to indicator D, 57 citations of 11 publications are presented, which give 104 points. It is obvious that the volume and quality of the scientific output for the acquisition of the scientific degree "Doctor of Sciences" exceeds the minimum requirements of the IEMPAM-BAN regulations for awarding scientific degrees and holding academic positions.

Conclusion

The "Doctor of Science" dissertation work of Associate Professor Silvia Nikolova is a detailed complex, interdisciplinary study for the purposes of which an innovative methodical approach using artificial intelligence was developed and applied, which guarantees the originality and reliability of the obtained results. The author revises the view that the metopic suture is not only a variation of the frontal bone and the phenomenon of metopism does not represent only a delay in the closure of the sutures. She developed a new hypothesis that metopism is associated with a specific configuration of the cranial vault, underdevelopment of the frontal sinus, extra bones and sutures. A clinical implication of this contribution is that persistent metopic suture should not be viewed solely as an accidental nonclosure of the metopic suture, but rather as an expression of a more general condition that, although rarely, has a clinical manifestation. Assoc. Prof. Nikolova's dissertation work is a contemporary base for further high-tech developments in the field of virtual anthropology and for the creation of a working group.

All this gives me sufficient ground for excellent assessment of the dissertation work of Assoc. Dr. Silvia Nikolova, entitled "Biomedical aspects of cranial sutures: microstructure, physiological closure, metopism" and strongly recommend to the members of the Scientific Jury to vote positively for awarding of the scientific degree "Doctor of Sciences" to Assoc. Silvia Nikolova in the specialty "Anthropology" 01.06.01, Professional field 4.3. "Biological Sciences".

A rectangular box with a black border, used to redact the signature of the professor. There are some blue ink scribbles around the box.

10.10.2023

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