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Annex No. 10 to the MU Directive on Habilitation Procedures and Professor Appointment Procedures

HABILITATION THESIS REVIEWER'S REPORT

Masaryk University	
Applicant	MUDr. Alena Damborská, Ph.D.
Habilitation thesis	Electrophysiological correlates of both resting-state mental activity and higher brain functions in humans (Methods of scalp and intracerebral electroencephalography)
Reviewer	Prof. Dr. med. habil. Markus Ullsperger
Reviewer's home unit, institution	Dept. of Neuropsychology, Institute of Psychology, Faculty of Natural Sciences Otto-von-Guericke University Magdeburg

[Review text]
Dr. Alena Damborská presents a cumulative habilitation thesis comprising fourteen original publications in international scientific journals. She is first, senior, and/or corresponding author in all but one of these publications. The thesis combines a set of original research studies and two review articles which all use electrophysiological recordings in humans, i.e., scalp-recorded electroencephalography (EEG) and intracranial recordings of local field potentials (LFPs) from implanted electrodes for diagnostic and therapeutic purposes separately and in combination. Dr. Damborská investigated spatio-temporal characteristics of event-related electrophysiological activity with the aim to contribute to the knowledge on neuronal substrate of non-motor and movement-related cognitive functions. Moreover, she explored the large-scale brain network dynamics during the resting state thereby focusing on the identification of abnormalities in affective disorders.

After an Introduction Section on the general aim of the thesis, the Methods Section gives a clear, comprehensive and concise overview about the methods applied in the studies comprised in this work, the underlying physiology of the neuronal signals, and advanced statistical techniques such as microstate analysis.

In Sections 3 and 5 the original studies are discussed and the according publications are added as annexes. Sections four and six report two reviews summarizing the utility of ERPs as biomarkers in pathological changes of brain functions due to trauma and the current knowledge on deep brain stimulation in neuropsychiatry.

Section 3.1 addresses the involvement of temporal and frontal brain areas in non-motor cognitive functions during a simple sensorimotor task. A prominent event-related potential (ERP) in the hippocampus was shown to occur independently of motor execution and is putatively related to stimulus evaluation. Moreover, the primary motor cortex was shown to be also active during non-motor functions. Section 3.2 comprises studies addressing the P300 ERP which demonstrate that this deflection is not only related to non-motor cognition but also to movement-related functions. Section 3.3 addresses motor-related functions and post-response monitoring after correct responses.

Section 5 is dedicated to interactions between brain regions and their characterization by means of electrophysiological recordings during rest. Coupling between subcortical structures and cortical areas was studied in a simultaneous intracranial and scalp EEG study revealing that the subthalamic nucleus is involved in bottom-up and top-down information flow. Three further studies address resting-state large-scale brain networks and their aberrant activity in affective disorders. Interestingly, increased resting-state connectivity of the amygdala suggests that this region might play an important and previously overlooked role in depression.

In a Conclusion section Dr. Damborska discusses the importance of her findings with a broader scientific perspective and demonstrates that EEG as well as invasive recordings have not lost their importance despite a nearly 100-year history. On the contrary, novel recording and analysis tools render this approach highly innovative and provide important insights that cannot be gathered with different neuroscientific techniques in humans.

Evaluation:
Dr. Damborska presents an impressive set of studies which are published in peer-reviewed scientific journals. Her work demonstrates that she is capable to lead a coherent and original research program. She has furthermore shown her proficiency with the relevant recording techniques as well as complex and advanced statistical analyses. Her research can be interpreted as translational as she links fundamental research projects revealing neuronal mechanisms in healthy humans with applied research in patients, e.g., with affective disorders. The thesis is clearly written, nevertheless I have listed a few questions for the scientific discussion below.
In summary, in my view this is a convincing habilitation thesis that has made important contributions to current research in cognitive and clinical neurosciences.

Reviewer's questions for the habilitation thesis defence (number of questions up to the reviewer)

1. Annex 3, Kukleta et al., Clin Neurophysiol, 2016: Electrophysiological activity was recorded from various intracranial electrodes/contacts using the right mastoid as a reference. The late component which was in the focus of this study was found at all channels including the contacts in the primary motor cortex. How can one be sure that this late component is generated near the recording contacts (e.g., in the motor cortex)? The source could also be somewhere else in the brain. Particularly, if it mainly affects the reference electrode, a large correlation across all recordings (as found in the study) would be expected. Which additional analysis could be done to support the inference that non-motor activity is generated in M1?

2. Annex 12, Damborská et al., Sci Rep, 2020: The main findings are related to deep (subcortical) structures, such as amygdala and caudate. Could you please elaborate on the sensitivity and precision of detecting electrophysiological activity of such structures (deep, closed-field configuration) in scalp-recorded EEG?

3. The method of microstate analysis of EEG data is interesting and has a long tradition. However, its use is limited to relatively few research groups. It would be interesting to discuss the commonalities and differences of this method with other source separation techniques such as independent component analysis, multivariate pattern analysis and others. What are the advantages of the microstates analysis? Can results be interpreted fundamentally differently than with other methods?

Conclusion

The habilitation thesis entitled “Electrophysiological correlates of both resting-state mental activity and higher brain functions in humans (Methods of scalp and intracerebral electroencephalography)” by MUDr. Alena Damborská, Ph.D. **fulfils** requirements expected of a habilitation thesis in the field of Neuroscience.

Date: 26.06.2023 Signature:

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