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Editorial

Advances in Depression Research

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Depressive disorders represent a common and disabling group of mental disorders. In the past decades, there has been achieved much progress in the research on the mechanisms and pathways underlying depression, including multiple levels of explanation and analysis [1]. There have been implicated molecular biomarkers of nitro-oxidative stress and immune-inflammatory pathways, detected in peripheral blood, and associated with major clinical features of disease [2]. Alterations in microstructure, dynamic functional and effective connectivity, and brain task-related functional magnetic resonance imaging studies contributed to producing an overarching biological "fingerprint" which may identify depressive disorder in terms of differential diagnosis with other psychotic or affective disorders [3].

This special issue is focused on integrative models that bring together clinical measures, with molecular, neurophysiological and brain imaging technologies to improve procedures and diagnostic criteria and critically inform treatment guidelines and protocols in psychiatry.

The reported results by Zhang and associates [4] suggest that the therapeutic mechanism of electroacupuncture (EA) combined with paroxetine is related to the regulation of the synaptic ultrastructure and regulating sirtuin 2/α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs) pathway in the hippocampal dentate gyrus of chronic unpredictable mild stress-induced depressive rats. This pre-clinical study is based on an animal model of mental disorder and the results from it should be interpreted in a cautious way, sensitive to the extrapolation and generalization in cross-species studies, when it comes to new evolutionary functions in cognitive and affective neuroscience [5].

Xiong et al. [6] performed a network analysis and simulation study to investigate the interference of physical activity and depression. The results suggest that moderate physical activity most strongly correlated with the course of depression. In addition, authors have identified certain gender differences, more specifically in men, interventions may prioritize increasing the regularity per week with moderate physical activity to prevent depression, whereas for women, focusing on the duration per day of such activity could be a promising target for complex management of major depression.

Kitov and associates [7] have explored the lipid and immune profile of patients diagnosed with metabolic syndrome (MetS). That contribution comes in a broader context [2] in which peripheral systemic immune-inflammatory and lipid metabolism factors are regarded as leading etiological complex for depression, reified by means of neurotoxic pathways. Constellations of LDL-C/ApoB ratio and IL-6 levels were found to be independently associated with depressive symptom severity in newly diagnosed MetS, highlighting their potential as clinically relevant biomarkers. These findings highlight perspectives for integrating lipid and inflammatory profiles in the stratification of depression risk within MetS populations.

In their replication study Agoalikum et al. [8] report advanced results, following earlier independent replication [9], of an innovative task-related functional magnetic resonance imaging (fMRI) paradigm design, where the task is constructed from diagnostically meaningful clinical self-evaluation scales. The original and replication studies represent complexity of functional network disruptions in depression and schizophrenia [8,10]. The emerging shared finding across studies determines precuneus as a relay hub whose network affiliation is modulated by task demands - default mode network engagement with posterior cingulate, and salience-executive network commitment when the diagnostic signal shifts to motor and cingulate regions instead. The receptor research provides insights to further explore that problem. Dopamine D2/D3 receptor binding potential in precuneus correlates with grey matter volume in healthy adults, including Brodmann areas 7 and 31, though the strongest coupling is actually in midbrain and cingulate [11]. That circuit's executive segment, dorsolateral prefrontal cortex is reported to have dopamine receptor subsystem abnormalities in schizophrenia [12], with possible interactions of dopamine and other, for instance, glutamatergic pathways.

This research calls for validation of the paradigm on another level of explanation: the molecular one, where the non-linear brain network dynamics during diagnostic task processing may be mapped in terms of the receptor density, e.g., derived from positron emission tomography atlases.

In a review, delivered by Barlattani and associates [13], there is provided insightful evidence that glymphatic-related MRI proxies, particularly diffusion tensor imaging

along the perivascular space (DTI-ALPS), are altered in depression. It is also concluded that DTI-ALPS may be considered as a rather indirect marker of perivascular diffusion rather than a direct measure of glymphatic flow. The reviewed evidence supports a careful translational framework for biomarker-informed trials and outlines the relevant phenotypes - a preliminary prognostic and theranostic biomarker for treatment-resistant depression.

Finally, the contribution of Skondra et al. [14] investigates the anticholinergic burden, as related to different aspects of the clinical phenotype of cognitive decline, including old age depression. Despite the lack of solid evidence regarding causal relationships and need for further research, minimizing anticholinergic burden in clinical settings is likely to deliver a potential pragmatic strategy in managing cognitive decline, comorbid with mood disorders in geriatric care.

In summary, the contributions from this Special Issue traverse a program for cross-validation of symptom scales against micro-level alterations (molecular signaling pathways), regional and network-level brain dysfunctions, and heterogeneous depressive spectrum phenotypes. This translational approach may be expanded in future towards mapping of the imaging data onto normative neuromediator atlases to better explain the underlying neurochemical mechanisms of disease.

Author Contributions

This is an individual contribution of DS. He conceived this Special Issue, edited it, wrote the draft of the Editorial, critically revised it, approved the final version for publication and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflicts of Interest

Drozdstoy Stoyanov is serving as one of the guest editors of this journal. We declare that Drozdstoy Stoyanov had no involvement in the process of this article and has no access to information regarding its process. Full responsibility for the editorial process for this article was delegated to Bettina Platt.

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