The World Journal of Biological Psychiatry

ISSN: 1562-2975 (Print) 1814-1412 (Online) Journal homepage: https://www.tandfonline.com/loi/iwbp20

Editorial

Maurizio Popoli(Field Editor)

To cite this article: Maurizio Popoli(Field Editor) (2020) Editorial, The World Journal of Biological Psychiatry, 21:8, 577-578, DOI: 10.1080/15622975.2020.1823693

To link to this article: https://doi.org/10.1080/15622975.2020.1823693

Published online: 22 Oct 2020.

THE WORLD JOURNAL OF BIOLOGICAL PSYCHIATRY
2020, VOL. 21, NO. 8, 577–578
https://doi.org/10.1080/15622975.2020.1823693

Editorial

Dear colleagues,

It is my great pleasure to introduce to you the eighth issue of 2020 featuring original research on depression, drug–drug interaction in psychiatric treatment of HIV, cannabinoid treatment of tardive dyskinesia, treatment of concurrent abuse of cocaine/nicotine and a review article on management of mild cognitive impairment (MCI).

Reduction of circulating brain-derived neurotrophic factor (BDNF) levels and increase of plasma dipeptidyl peptidase-4 (DPP4) activity have both been reported to link to the pathogenesis of depression. Zheng and colleagues explored the **correlation between the ratio DPP4 activity/BDNF levels (DBR) and depressive symptoms** as a biomarker for depression. In general, DPP4 activity was negatively correlated to BDNF levels in participants with and without depression. Depressed patients had lower levels of BDNF and higher DPP4 activity and DBR in peripheral circulation when compared with controls. The results suggested that the positive correlation between DBR and depressive symptoms identify DBR as a novel biological marker or a possible therapeutic target for depression.

Lee et al. found that **detection of intracellular cytokines after lipopolysaccharide (LPS) stimulation of monocytes in vitro rather than simple measurement of circulating cytokines** may be more sensitive correlates of subthreshold depressive symptoms. Circulating inflammatory markers have been correlated with mood disorders, but often no changes are found in case-control studies (Mucci et al. 2020). They measured plasma tumour necrosis factor-α (TNF- α), interleukin-6 (IL-6) and C-reactive protein (CRP), and *in vitro* LPS-induced monocyte production of IL-6 and TNF- α, in 117 participants to a cross-sectional insomnia study in a healthy community-dwelling older adults. Multivariate linear regression was conducted to test the associations between inflammatory markers and subthreshold depressive symptoms in the entire sample, as well as in subgroups stratified into higher and lower inflammation levels. In the entire sample, no circulating biomarkers were significantly associated with subthreshold depressive symptoms. Instead, LPS-induced cytokines significantly and positively correlated with subthreshold depressive symptoms in higher inflammation subgroups. The authors concluded that LPS-induced cytokines may be more sensitive correlates of subthreshold depressive symptoms than circulating cytokines, particularly in older adults with higher systemic inflammation.

The management of psychiatric illness in HIV-infected patients is clinically challenging because of the risk of potential drug–drug interactions. Cattaneo and associates aimed to measure the **anti- depressant and/or antipsychotic drug concentrations in HIV-infected patients during routine outpatient visits**. Six hundred HIV-infected patients were screened during the first 15 months after the introduction of outpatient polytherapy management service. The distribution of psychotropic drug concentrations in HIV-infected patients was compared with that observed in a control group of HIV-negative patients monitored over the same period. Fifty-five per cent of patients receiving concomitant antiretroviral and psychotropic drug treatment had plasma psychotropic drug concentrations that were below minimum effective levels, compared to 26% of HIV-negative patients. The results were not affected by patients' gender, age, adherence to therapies or drug–drug interactions and showed that psychotropic drug treatments are associated with a higher rate of subtherapeutic concentrations in HIV-infected patients. The possible reasons for this finding in HIV-infected patients are analysed.

Lateral habenula (LHb) is a key brain structure for mediating behavioural responses to aversive stimuli and recently hyperactivation of this area has been involved in pathophysiology of depression (Cui et al. 2018). LHb receives presynaptic inputs from ventral pallidum (VP) which relates to reward, motivation and hedonics. Liu and colleagues investigated the role of glutamatergic VP-LHb projections in negative emotions and depressive-like behaviour, using optogenetic manipulation in mice. Activation of VP-LHb glutamatergic projections induced aversive behaviour in the real time place aversion test. In mice subjected to chronic social defeat stress (a stress protocol used to induce depressive/anxious-like behaviour), optogenetic activation of this circuit induced depressive-like phenotype, while inhibition of the circuit exerted antidepressant effect in social stress susceptible mice. Local injection of ketamine into LHb rescued the depressive-like phenotype caused by activation of this circuit. The results of the study demonstrated an involvement of the glutamatergic VP-LHb circuit in stress-induced depression-related behaviours and in the antidepressant action of ketamine.

Movement disorders, such as tardive dyskinesia (TD), are associated not only with typical and atypical antipsychotics, but also with levodopa treatment, although they are more common in patients on typical antipsychotics. Kajero and associates investigated the **effects of oral**

cannabidiol (CBD; the most abundant non-psychotomimetic compound in *Cannabis*, which has raised much interest for its putative therapeutic actions in CNS; Khoury et al. 2019) on TD. They assessed haloperidol-induced vacuous chewing movements (VCM) in rats, an animal model of TD. Rats were administered haloperidol only or haloperidol + CBD at various doses between 3 and 10 mg/kg. The results showed that CBD co-administration with haloperidol at different doses attenuated the VCMs and increased motor tone produced by haloperidol. CBD also ameliorated haloperidol-induced increased blood glucose levels. CBD alone at 5 mg/kg showed anxiolytic properties. This work confirmed that CBD can ameliorate motor impairments produced by haloperidol. The data suggest that CBD could be combined with haloperidol to prevent the emergence of extrapyramidal side effects and long-term movement disorders, such as acute dystonic disorder and TD.

The review by Kasper et al. addresses **the issue of management of mild cognitive impairment** (MCI). The authors aim to describe the **concept of MCI with regard to diagnosis, pathogenesis and treatment, review the evidence of available pharmacological and non-pharmacological treatments for MCI**, and analyse respective information and limitations in national and international guidelines. Consensus diagnostic criteria for MCI are available; early recognition and accurate classification of MCI subtypes is possible. Operational use of biomarkers for amyloid pathology and neuronal injury allows to differentially assess the likelihood of progression to Alzheimer's disease (AD) dementia at the MCI stage, including cerebrospinal fluid concentrations of amyloid beta 42, phospho-tau/total tau protein, and several blood-based biomarkers (Lewczuk et al. 2018). Mixed pathologies are the rule in MCI, thus a multi-target treatment approach is a rational strategy. Promising evidence has been generated for multi-domain interventions. Limited evidence is available for different pharmacological classes that have been investigated in MCI clinical trials (e.g. acetylcholinesterase inhibitors). EGb 761VR treatment improved symptoms in some clinical trials and is currently the only pharmacological treatment recommended in existing guidelines for the symptomatic treatment of MCI. Recent national guidelines are only just beginning to consider pharmacological and non-pharmacological treatment options for patients with MCI. However, recommendations reported in international and national dementia guidelines are inconsistent and do not consider the recent diagnostic concepts, nor the most recent pharmacological and non-pharmacological treatment evidence. The role of biomarkers as a tool for diagnosing the MCI stage of AD is not considered; and treatment outcomes in MCI only focus on the lack of risk reduction for progression to dementia. In order to improve management of MCI and recognise the importance of this disease stage within the AD continuum, it is necessary to update existing guidelines with respect to available evidence.

Barbosa-Mendez and colleagues assessed **the use of mirtazapine to reduce the reinforcing effects of concurrent use of cocaine and nicotine**. Concurrent abuse of cocaine and nicotine is considered a public health problem, but no effective therapy is available. Mirtazapine is an antagonist of the α2-adrenoceptor and 5-HT2A/C and 5-HT3 receptors, and has been shown to reduce cocaine, nicotine and methamphetamine behavioural effects in humans and animals. The study evaluated the effect of mirtazapine on the enhancement of locomotor activity during the induction and expression of cocaine and nicotine-dependent locomotor sensitisation. Wistar rats were dosed with cocaine, nicotine or cocaine + nicotine combination. Mirtazapine was administered during the extinction phase. Mirtazapine decreased cocaine + nicotine-induced locomotor activity and induction and expression of locomotor sensitisation. In addition, co-administration of mecamylamine and mirtazapine significantly enhanced the effect of mirtazapine. The result suggest that mirtazapine shows efficacy in decreasing the psycho-stimulant effects of concurrent use of cocaine and nicotine.

ORCID

Maurizio Popoli http://orcid.org/0000-0003-4670-8664

References

Cui Y, Yang Y, Ni Z, Dong Y, Cai G, Foncelle A, Ma S, Sang K, Tang S, Li Y, et al. 2018. Astroglial Kir4.1 in the lateral habenula drives neuronal bursts in depression. Nature. 554(7692):323–327.

Khoury JM, Neves M. d C L d, Roque MAV, Queiroz D. A d B, Corrêa de Freitas AA, de Fátima Â, Moreira FA, Garcia FD. 2019. Is there a role for cannabidiol in psychiatry? World J Biol Psychiatry. 20(2):101–116.

Lewczuk P, Riederer P, O'Bryant SE, Verbeek MM, Dubois B, Visser PJ, Jellinger KA, Engelborghs S, Ramirez A, Parnetti L, on Behalf of the Members of the WFSBP Task Force Working on this Topic: Peter Riederer, Carla Gallo, Dimitrios Kapogiannis, Andrea Lopez Mato, Florence Thibaut, et al. 2018. Cerebrospinal fluid and blood biomarkers for neurodegenerative dementias: An update of the Consensus of the Task Force on Biological Markers in Psychiatry of the World Federation of Societies of Biological Psychiatry. World J Biol Psychiatry. 19(4):244–328.

Mucci F, Marazziti D, Della Vecchia A, Baroni S, Morana P, Carpita B, Mangiapane P, Morana F, Morana B, Dell'Osso L. 2018. Inflammatory and metabolic markers in patients with mood disorders. World J Biol Psychiatry. 2020 Jun 18:1–8. doi: 10.1080/15622975.2020.1775891. Online ahead of print.

Yours sincerely,

Maurizio Popoli, PhD
Field Editor
maurizio.popoli@unimi.it