

multicentric study on safety and effectiveness (REAL-ESK study). *Journal of Affective Disorders* 319, 646–654. [3] Samalin, L., Rothärmel, M., Mekaoui, L., Gaudré-Wattinne, E., Codet, M.-A., Bouju, S., Sauvaget, A., 2022. Esketamine nasal spray in patients with treatment-resistant depression: the real-world experience in the French cohort early-access programme. *International Journal of Psychiatry in Clinical Practice* 1–11. [4] Brendle, M., Ahuja, S., Valle, M., Moore, C., Thielking, P., Malone, D., Robison, R., 2022. A Real-World Retrospective Study Evaluating Safety, Effectiveness, and Cost of Intranasal Esketamine for Treatment-Resistant Depression. *Abstract. Value in Health* 25, S313. No conflict of interest

doi: <https://doi.org/10.1016/j.nsa.2023.103906>

P.1137

NEUROSCIENCE APPLIED 2 (2023) 102441 103907

IS CHRONIC FATIGUE SYNDROME A NOVEL NAME FOR ATYPICAL DEPRESSION? DISCUSSION FROM A MONOAMINE OXIDASE INHIBITORS SUCCESSFUL CASE

D. Carmona-Farres¹, R. Lopez-Escribano¹. ¹ Vic Hospital Consortium, Psychiatry and Mental Health Department, Vic, Spain

Background: Chronic Fatigue Syndrome (CFS) is a chronic syndrome characterized by generalized pain and cognitive symptoms without a recognized histopathological injury. Among comorbidities, depression is common. Depression increases the risk of CFS being diagnosed, and in turn CFS increases the risk of depression. Common physiopathological pathways can be found both in FM and depression, such as alterations of glucocorticoid hormonal axis or neuro-inflammation [1]. In CFS, atypical depression is 1.5 times more common than melancholic depression [2]. Monoamine oxidase inhibitors (MAOIs) have been found effective in CFS [3]. Objective: To essay whether MAOIs (a) are effective in the treatment of depressive symptoms in FM, (b) the degree of improvement of fibromyalgia symptoms with the use of MAOIs, (c) how a MAOIs treatment affects functioning, general Quality of Life (QoL) and treatment-related QoL, and (d) side-effect profile of MAOIs in FM and depression comorbidity.

Methods: Clinical case narrative exposition with a review of clinical notes as well as end-point scale evaluation. We used Hamilton Depression Rating Scale (HDRS), Inventory of Depressive Symptomatology Self-Rated (IDS-SR30) to quantify depressive symptoms, Functioning Assessment Short Test (FAST) to evaluate functioning, Health Survey Short-Form (SF-36) to study general QoL and Evaluation of Antidepressant Treatment Satisfaction (ESTA) to measure treatment-related QoL; and Udalvalg for Kliniske Undersøgelser (UKU) to delimitate side-effects profile. All scales are validated in Spanish population. Informed consent were collected. **Results:** A 65-year-old woman patient seek medical attention for a 30 year-long CFS with notable cognitive and sleep disturbances. The patient showed a pharmacological resistance, with a history of multiple antidepressants (Vortioxetine, Fluoxetine, Nortriptyline and Trazodone), stimulants (Modafinil) and anxiolytics (Alprazolam and Lormetazepam) treatment essays, none of them achieving significant clinical improvement. During evaluation, a clinical picture of sadness, apathy, abulia, leaden paralysis, mood reactivity and an interpersonal rejection sensibility was shown. With these symptoms in mind, atypical depression was considered as a plausible explanation, and therefore Phenelzine treatment was suggested. After a 4-week wash-off period, Phenelzine was initiated at 15 mg o.d. After one week, Phenelzine was up titrated to 30 mg o.d., and then to 45 mg o.d. after another week. Patient reported a noticeable improvement of anxiety symptoms after the first week and a clearly significant improvement of depressive mood, abulia and apathy 3 weeks after the start of Phenelzine, with a decrease in fatigue and cognitive complaints. A scale evaluation was scheduled 2.5 months after the start of Phenelzine. Clinical depression was mild (total points: 8) based on HDRS and moderate-severe (total points: 37) with IDS-SR30 criteria. Daily functioning showed most impairment in cognitive and work-related areas. General QoL highlighted role limitations due to physical health problems (relative score: 0), and treatment-related QoL was excellent (total score 9). Side-effects profile was mild with only xerostomia (severity score: 2) and weight gain (severity score: 3) described.

Conclusion: CFS and atypical depression share common clinical and physiopathological features, such as severe fatigue, cognitive impairment and neuro-inflammation. MAOIs can be considered in treatment-resistant FM, specially when atypical depression symptoms are present.

References

[1] Yepez, D., Grandes, X. A., Talanki Manjunatha, R., Habib, S., & Sangaraju, S. L. (2022). Fibromyalgia and Depression: A Literature Review of Their Shared

Aspects. *Cureus*, 14(5), e24909. <https://doi.org/10.7759/cureus.24909> [2] Ross, R. L., Jones, K. D., Ward, R. L., Wood, L. J., & Bennett, R. M. (2010). Atypical depression is more common than melancholic in fibromyalgia: an observational cohort study. *BMC musculoskeletal disorders*, 11, 120. <https://doi.org/10.1186/1471-2474-11-120> [3] Tort, S., Urrútia, G., Nishishinya, M. B., & Walitt, B. (2012). Monoamine oxidase inhibitors (MAOIs) for fibromyalgia syndrome. *The Cochrane database of systematic reviews*, (4), CD009807. <https://doi.org/10.1002/14651858.CD009807>.

No conflict of interest

doi: <https://doi.org/10.1016/j.nsa.2023.103907>

P.1138

NEUROSCIENCE APPLIED 2 (2023) 102441 103908

CROSSTALK ACROSS BARRIERS: CHOROID PLEXUS VOLUME AFFECTS WHITE MATTER INTEGRITY IN BIPOLAR DEPRESSION

B. Bravi^{1,2}, E.M.T. Melloni¹, M. Paolini^{1,3}, M. Biondi¹, C. Colombo^{4,5}, R. Zanardi^{4,5}, F. Benedetti^{1,4}. ¹ IRCCS Scientific Institute Ospedale San Raffaele, Psychiatry & Clinical Psychobiology Unit- Division of Neuroscience, Milan, Italy; ² University Vita-Salute San Raffaele, Psychology- PhD program in Cognitive Neurosciences, Milan, Italy; ³ University Vita-Salute San Raffaele, Neuroscience- PhD program in Molecular Medicine, Milan, Italy; ⁴ Vita-Salute San Raffaele University, Neuropsychiatric Sciences, Milan, Italy; ⁵ IRCCS Ospedale San Raffaele, Department of Affective Disorders- Mood Disorders Unit, Milan, Italy

Background: Choroid plexus (CP) is a physiological barrier, producing cerebrospinal fluid (CSF), neurotrophic, and inflammatory factors. It's involved in the neuro-immune axis, facilitating the interplay between central and peripheral inflammation, allowing trafficking of immune cells. Coherently, CP enlargement has been found in pathological conditions characterized by inflammatory signature, including mood disorders [1]. More specifically, CP volume was correlated with the amounts of white matter (WM) lesions in multiple sclerosis [2], and it was correlated with central microglia activation in major depressive disorder [3], suggesting an increasing trafficking across parenchyma and periphery. It becomes crucial to understand the possible role of CP enlargement in WM integrity disruption in bipolar disorder (BD) in order to better elucidate ongoing immune mechanisms fostering the psychopathology.

Methods: We studied 70 BD depressed patients and 50 age- and sex-matched healthy controls (HCs). We assessed differences in the left and right CP volume between the two groups in the context of the Generalized Linear Model (GLMZ) accounting for total intracranial volume (ICV). Diffusion Weighted Images (DWI) were acquired on a 3-Tesla scanner for the BD sample, while T1-weighted images for both samples. CP was segmented and volume was extracted using FreeSurfer 6.0. Diffusion Tensor images (DTI) correction, analysis, and tensor calculations were carried out with FSL 6.0. Next, using Tract-Based Spatial Statistics [4] individual tract invariant skeletons for each participant were obtained. The skeletons were then fed into voxel-wise nonparametric permutation-based cross-subject statistics, as implemented in Randomise FSL's tool. We tested for linear effects of left and right CP volume on Fractional Anisotropy (FA), Mean (MD), Axial (AD), and Radial Diffusivity (RD) across the WM skeleton with general linear models (GLM), accounting for the effects of age, sex, ICV, and lithium treatment. Threshold-free cluster enhancement (TFCE) was used.

Results: Statistical analyses revealed that BD patients had significantly greater bilateral CP volume compared with HCs (Left: $LR \chi^2 = 12.434$, $p < 0.001$; Right: $LR \chi^2 = 8.232$, $p = 0.004$). DTI regressions highlighted a significant negative association of both left and right CP volume with FA (Left: $p = 0.004$; Right: $p = 0.002$), and a positive one with AD (Left: $p < 0.001$; Right: $p < 0.001$), RD (Left: $p = 0.004$; Right: $p = 0.004$), and MD (Left: $p = 0.006$, Right: $p = 0.005$) in BD. Significant findings included a widespread pattern of WM tracts encompassing: corpus callosum, bilateral corona radiata (anterior, superior, and posterior), bilateral cingulate gyrus, bilateral superior longitudinal fasciculus, bilateral superior and inferior fronto-occipital fasciculi, fornix, bilateral anterior and posterior limbs of internal capsule, and bilateral posterior thalamic radiation.

Conclusion: This is the first finding pointing out the effect of CP enlargement on WM alterations in patients with BD. A widespread pattern of negative association with FA associated with positive ones with RD, MD, and AD may indicate a general WM suffering in condition of greater CP volume and immune system alterations. In particular, these results could clarify the role of immune system cross-talk between central and peripheral inflammation, supporting the hypothesis of a heightened trafficking of immune mediators that may underlie an inflammation-resolving mechanism in the central nervous system [5].

References

[1] Goldsmith, D.R., Rapaport, M.H., Miller, B.J., 2016. A meta-analysis of blood cytokine network alterations in psychiatric patients: comparisons between schizophrenia, bipolar disorder and depression. *Mol Psychiatry* 21, 1696–1709. [2] Chen, X., Luo, D., Zheng, Q., Peng, Y., Han, Y., Luo, Q., Zhu, Q., Luo, T., Li, Y., 2023. Enlarged choroid plexus related to cortical atrophy in multiple sclerosis. *Eur Radiol* 33, 2916–2926. [3] Althubaity, N., Schubert, J., Martins, D., Yousaf, T., Nettis, M.A., Mondelli, V., Pariante, C., Harrison, N.A., Bullmore, E.T., Dima, D., Turkheimer, F.E., Veronese, M., 2022. Choroid plexus enlargement is associated with neuroinflammation and reduction of blood brain barrier permeability in depression. *Neuroimage Clin* 33, 102926. [4] Smith, S.M., Jenkinson, M., Johansen-Berg, H., Rueckert, D., Nichols, T.E., Mackay, C.E., Watkins, K.E., Ciccarelli, O., Cader, M.Z., Matthews, P.M., Behrens, T.E., 2006. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage* 31, 1487–1505. [5] Schwartz, M., Baruch, K., 2014. The resolution of neuroinflammation in neurodegeneration: leukocyte recruitment via the choroid plexus. *EMBO J* 33, 7–22.

Conflict of interest:

Research activities are supported by the Italian Ministry of Health, GR-2018-12367789

doi: <https://doi.org/10.1016/j.nsa.2023.103908>

P.1139

NEUROSCIENCE APPLIED 2 (2023) 102441 103909

EXPOSURE TO DELTA9-THC DURING LACTATION MODULATES THE EFFECTS OF ALLOPREGNANOLONE TREATMENT IN A MICE MODEL OF POSTPARTUM DEPRESSION

P. Berbegal Sáez¹, A. García-Baos^{1,2}, O. Valverde^{1,2}. ¹ *Universitat Pompeu Fabra, Department of Medicine and Life Sciences, Barcelona, Spain*; ² *IMIM, Hospital Del Mar Research Institute, Barcelona, Spain*

Postpartum depression (PPD) is a serious psychiatric disorder that affects a significant percentage of women during pregnancy and the postpartum period [1]. Its negative consequences for both, mothers and newborns make it a Public Health issue. Cannabis is the most used illicit drug worldwide, and there is a growing trend of its use during the perinatal period, in part due to the perception that it is a safer alternative for treating pregnancy-related symptoms. However, postpartum cannabis use is associated with depressive effects in mothers and problems in newborn's development [2]. Our study aimed to investigate in a mouse model of PPD whether delta-9-tetrahydrocannabinol (THC) exposure during lactation would alter the efficacy of allopregnanolone, the actual prescribed treatment for this disorder.

We elicited PPD-like behaviour in C57BL/6 mice through maternal separation with early weaning (MSEW) [3], and then administered THC (2 mg/kg/day, ip) or vehicle during lactation (17 or 21 days for MSEW or SN groups respectively). On postnatal day 3, maternal behaviour was assessed by pup retrieval test. PPD traits, including anxiety, despair-behaviour, anhedonia and social behaviour, were assessed 24 hours after separate the offspring. Dams were treated after weaning with alloprenanolone (2mg/kg, ip) or vehicle 30 min before the experiments.

In the pup retrieval experiment, all SN lactating females retrieved all the pups, whereas less than 25% of MSEW-VEH females retrieved them (Logrank test, $p < 0.05$). Furthermore, MSEW-VEH mice showed larger dispersion of the pups from the nest centroid (ANOVA, $p < 0.05$) and disrupted digging behaviour (ANOVA, $p < 0.001$). Interestingly, THC exposure changed mothers' performance, almost reaching to 80% of MSEW dams who retrieved all pups. After weaning, MSEW dams showed increased immobility time (t-test, $p < 0.05$) evaluated in tail suspension test and increased anxiety-like behaviour (t-test, $p < 0.05$) assessed in the elevated plus maze. Both, allopregnanolone and THC (ANOVA, $p < 0.05$) decreased the despair-like behaviour in MSEW postpartum mice. However, the animals exposed to both treatments did not exhibit any behavioural improvement, indicating a possible effect of perinatal exposition to THC in allopregnanolone treatment effectiveness. Anhedonia was analysed in splash test, vehicle-treated MSEW dams displayed less self-grooming behaviour compared to SN females (t-test, $p < 0.01$), however any treatment was effective in mitigating anhedonic symptoms. The results of the social interaction test revealed no significant differences between the groups, suggesting that maternal separation did not have an impact on sociability in this mice model. Ongoing investigations include additional tests to thoroughly evaluate anxiety levels, potential cognitive impairments, and the effects of THC and allopregnanolone

treatments on different behaviours within PPD model.

Our results indicate a potential interplay between THC and allopregnanolone in individuals exhibiting symptoms of PPD. The findings from this research hold significant relevance for informing clinical guidelines and emphasize the importance of taking into account cannabis use in this specific population. This extends beyond the scope of PPD diagnosis and also involves the prescription of suitable treatment strategies for postpartum depression.

References

[1] American Psychiatric Association, 2013. Diagnostic and statistical manual of mental disorders, fifth ed. American Psychiatric Association Publishing, Washington [2] Ko, J. Y., Farr, S. L., Tong, V. T., Creanga, A. A., & Callaghan, W. M., 2015. Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. *American journal of obstetrics and gynecology*, 213(2), 201.e1–201.e10. [3] García-Baos, A., Gallego-Landin, I., Ferreres-Álvarez, I., Puig-Reyne, X., Castro-Zavala, A., Valverde, O., & Martín-Sánchez, A., 2022. Effects of fast-acting antidepressant drugs on a postpartum depression mice model. *Biomedicine & pharmacotherapy*, 154, 113598.

No conflict of interest

doi: <https://doi.org/10.1016/j.nsa.2023.103909>

P.1140

NEUROSCIENCE APPLIED 2 (2023) 102441 103910

REAL-WORLD PRESCRIPTION PATTERN AND AUGMENTATION OF ATYPICAL ANTIPSYCHOTICS IN MAJOR DEPRESSIVE DISORDER ACROSS EUROPEAN COUNTRIES: A SYSTEMATIC LITERATURE REVIEW

D. Hadzi Boskovic¹, B. Talon², B. Singh³, S. Attri³, M. Miguez⁴, F. Ardici⁵. ¹ *Otsuka Pharmaceutical Development & Commercialization Inc., Global Value and Real World Evidence, Princeton, United States*; ² *Lundbeck LLC, Global Health Economics and Outcomes Research, Deerfield, United States*; ³ *Pharmacoevidence, Health Economics and Outcome Research, SAS Nagar Mohali, India*; ⁴ *Otsuka Pharmaceutical Development & Commercialization Inc., Global Medical Affairs, Princeton, United States*; ⁵ *H. Lundbeck A/S, Global Medical Strategy and Communication, Copenhagen, Denmark*

Background: Only 30% of major depressive disorder (MDD) patients achieve remission with available antidepressant therapy (ADT). Improved understanding of using atypical antipsychotics (AAPs) for MDD, adhering to guidelines, and global variations is needed among healthcare providers.

Aim: A systematic literature review (SLR) was undertaken to understand the treatment guidelines (TGs), initial ADT patterns, switching, discontinuations, and augmentation with AAPs for the treatment of adult patients with MDD in Europe.

Methods: Embase, MEDLINE, CENTRAL, and PsycINFO were searched for English language studies published between inception to Dec 2022, reporting the prescription patterns and management guidelines. The SLR followed the standard methodology for conducting reviews as per Cochrane Handbook and PRISMA guidelines.

Results: Of 5,449 citations screened, four treatment guidelines (TGs), and 17 real-world treatment pattern (TP) studies met the eligibility criteria. The TGs were available for the UK (NICE 2022; BAP 2008), Germany (S3 2011), and France (AFPPN-FondaMental 2019). The TP studies were conducted across European countries namely the UK (n=2), Germany (n=1), Italy (n=5), Belgium (n=1), Denmark (n=1), Finland (n=2), Hungary (n=1), Spain (n=1), and multiple countries (n=3). The sample size ranged from 71 to 224,353 and the follow-up ranged from 3 months to 3.3 years. All included guidelines recommend selective serotonin reuptake inhibitors (SSRIs)/serotonin-norepinephrine reuptake inhibitors (SNRIs) as first-line treatments for MDD and the real-world prescription patterns align with this recommendation. SSRIs (n=10; median 62.81%, range 42.98% to 93.0%) are the most prescribed initial treatment followed by SNRIs (n=10; median 23.04%, range 1.0% to 81%). Further, the most frequently utilised ADTs were citalopram, escitalopram, paroxetine, sertraline, and fluoxetine. Discontinuation from initial ADTs was reported by four studies (median: 50.25%, range 12.9% to 71.9%) with lost to follow-up being the most common reason (68.7%; n=1). TGs suggest switching to another ADT, combination (initial ADT + other ADT), or AAP augmentation (initial ADT + AAP) for MDD patients who failed initial ADT. Except for Germany, all TGs recommend augmentation with AAP after no or partial response to initial ADTs. AAP augmentation reported among the seven studies ranged from 1.33% (N=2,24,353) to 47.17% (N=349). Regarding line of therapy (LOT) distribution, AAP augmentation was utilised by 0.07% and 20.80% of patients in LOT 1 (n=2), by 47.17% in LOT 2 (n=1), by