studies), week 10 (2 studies), or week 12 (2 studies). Baseline HAM-D item scores were standardized and included in the cluster analysis, which used Ward's minimum variance method to define distance. Efficacy versus placebo was assessed based on change from baseline in HAM-D17 total score, and response and remission rates. HAM-D17 total score at week 8/last-observation-carried-forward (LOCF) was analyzed using an analysis of covariance (ANCOVA) model with terms for study, treatment, cluster, interaction of treatment and cluster, and baseline HAM-D17 total score. Logistic regression models were used for the analysis of response and remission rates at week 8/LOCF with the same terms that were used for the ANCOVA model.
Results: A total of 2599 patients from 9 trials had complete data and were included in the cluster analysis. The study population was 60% female and 71% white; most patients were moderately (59%) or markedly (31%) ill at baseline. Three patient clusters were identified based on baseline HAM-D item scores. The majority of patients (77%) fell in cluster 1, characterized by core symptoms and low anxiety (baseline HAM-D17 total score=23). Cluster 2 (12%) had mild core symptoms with low anxiety (baseline HAM-D17 total score=20.6), and cluster 3 (11%) had core symptoms with high anxiety (baseline HAM-D17 total score=27.4). For clusters 1 and 3, significant effects of venlafaxine versus placebo were observed on the change from baseline in HAM-D17 total score at week 8/LOCF; adjusted mean (standard error [SE]) difference from placebo was −2.71 (0.35) for cluster 1 and −3.67 (0.89) for cluster 3 (both $P<0.001$). There were no significant treatment effects on HAM-D17 total score outcome for cluster 2 (adjusted mean (SE) difference, −0.77 [0.85]). Similarly, significant treatment effects on rates of response and remission at week 8/LOCF were observed for clusters 1 and 3, but not for cluster 2.
Conclusions: Among 2599 MDD patients in 9 venlafaxine studies, 3 unique clusters of patients were identified based on HAM-D17 item scores at baseline. The clusters differed in their baseline core symptoms and level of anxiety, and may predict efficacy outcomes in patients treated with venlafaxine.

Disclosure statement: Full-time employee of Pfizer Inc and holds Pfizer stock and stock options

doi: 10.1016/j.euroneuro.2019.09.594

P.611 Biomarkers of inflammation and neural plasticity in olfactory neuroepithelium-derived cells from patients with major depressive disorder

P. Álvarez[1], J.M. Gines[1,*], C. Fernández[2], A. Toll[1], C. Díez-Aja[1], L.M. Martín[1], V. Pérez-Solá[1], R. De la Torre[2], V. Soria[3], P. López-García[4], P. Robledo[2]

[1] *Institute of Neuropsychiatry and Addictions- Hospital del Mar- IMIM- Barcelona- Spain., Psychiatry, Barcelona, Spain*
[2] *IMIM-Hospital del Mar Medical Research Institute, Integrative Pharmacology and Systems Neuroscience, Barcelona, Spain*
[3] *Bellvitge University Hospital- Bellvitge Biomedical Research Institute IDIBELL Neurosciences Group-Psychiatry and Mental Health, Psychiatry, Hospitalet de Llobregat Barcelona, Spain*
[4] *Universidad Autónoma, Psychiatry, Madrid, Spain*

Background: Growing evidence suggests a significant role of inflammation and neural plasticity processes in the pathogenesis of major depressive disorder (MDD) [1,2]. The olfactory mucosa has great potential as a tool to examine neurophysiological processes in psychiatric disorders, as its sensory neurons are replaced by neurogenesis continuously throughout adult life from neuronal precursor/progenitors. Thus, this accessible tissue closely related to the central nervous system, can allow the non-invasive, low-cost study of new biomarkers and therapeutic targets for neuropsychiatric diseases. Studies in cell cultures obtained from the olfactory neuroepithelium (ON) of patients with several different types of neuropsychiatric disorders show specific alterations in cellular function [3]. However, few studies are available using this methodology to study novel biomarkers of MDD.
Objective: The aim of this study was to determine the diagnostic value of inflammatory and neural plasticity markers (MAPK14, IL6, TNF-a, Mecp2, BDNF, GSK3, GRIA2 and FosB) in MDD, and to study the relationship between these biomarkers and course, clinical and psychometric variables. Methods: Twelve patients with MDD, according to DSM-IV criteria and seven psychiatrically healthy controls were included. Patients and controls were assessed with MINI interview for the exclusion of other mental disorders (patients) or any mental disorder (controls). Inflammatory diseases were considered exclusion criteria. Demographical, course and clinical variables were recorded. Treatment-resistant scores were classified using the Thase and Rush staging method. Psychometric assessment included Hamilton Depression Rating Scale (HDRS), The State-Trait Anxiety Inventory (STAI), The Holmes-Rahe Social Readjustment Rating Scale, The Perceived Stress Scale (PSS), Global Assessment of Functioning (GAF) and World Health Organization Disability Assessment Schedule (WHODAS 2.0). mRNA was isolated from ON cells and MAPK14, IL6, TNF-a, Mecp2, BDNF, GSK3, GRIA2 and Fos-B gene expression levels were quantified using quantitative polymerase chain reaction (q-PCR). Multivariate regression analyses were performed to test the association between mRNA levels of these biomarkers and disease course, clinical and psychometric variables.
Results: The results showed lower mRNA levels of BDNF, GSK3 y GRIA2 in MDD patients in comparison with controls. Fos-B mRNA levels were significantly higher in male patients in comparison with female patients, and with male controls, whereas GSK3 mRNA levels were significantly lower in female patients in comparison with female controls. In the total sample, BDNF mRNA levels were negatively correlated with perceived stress and state anxiety. Specific associations in the patient group and not in the control group were found for GRIA2 and IL6 mRNA, which were positively correlated with age, and for BDNF and IL6 mRNA levels which were negatively correlated with the perceived stress score.
Conclusion: These results reveal specific BDNF, GRIA2 and Fos-B gene expression changes in ON cells of depressed patients, suggesting that (i) these biomarkers of neural plasticity could be relevant as diagnostic tools for MDD,

(ii) sex should be taken into account when studying Fos-B and GSK3 expression in ON cells, and (iii) the ON is a good cellular model to study the neurobiological mechanisms contributing to mental disorders.

Disclosure statement: This abstract is partially funded by the Instituto de Salud Carlos III (Ministry of Economy and Competitiveness) (FEDER PI15/0039)

References

[1] Leonard, B.E., 2018. Inflammation and depression: a causal or coincidental link to the pathophysiology? Acta Neuropsychiatrica 30 (1), 1–16.
[2] Liu, W., Ge, T., Leng, Y., Pan, Z., Fan, J., Yang, W., Cui, R., 2017. The Role of Neural Plasticity in Depression: From Hippocampus to Prefrontal Cortex. Neural Plast.
[3] Lavoie, J., Gassó Astorga, P., Segal-Gavish, H., Wu, Y.C., Chung, Y., Cascella, N.G., Sawa, A., Ishizuka, K., 2017. The Olfactory Neural Epithelium As a Tool in Neuroscience. Trends Mol Med 23 (2), 100–103.

doi: 10.1155/2017/6871089

P.612 Symptom network structure differences in acute depression between bipolar disorder and major depressive disorder: A network analysis.

G. Anmella [1,*], F. Corponi [2], I. Pacchiarotti [1], N. Verdolini [1,3,4], L. Samalin [5], D. Popovic [6], J.M. Azorin [7], J. Angst [8], C.L. Bowden [9], S. Mosolov [10], A.H. Young [11], G. Perugi [12], E. Vieta [1], A. Serretti [2], A. Murru [1]

[1] *Institute of Neuroscience, Bipolar and Depressive Disorders Unit- Institute of Neuroscience- Hospital Clinic- University of Barcelona- IDIBAPS- CIBERSAM- 170 Villarroel st-12-0- 08036, Barcelona- Catalonia- Spain, Spain*
[2] *University of Bologna, Department of Biomedical and Neuromotor Sciences, Bologna, Italy*
[3] *University of Perugia, Division of Psychiatry- Clinical Psychology and Rehabilitation- Department of Medicine- Santa Maria della Misericordia Hospital- University of Perugia- Ellisse Building- 8th Floor- Sant'Andrea delle Fratte- 06132, Perugia- Italy*
[4] *FIDMAG, FIDMAG Germanes Hospitalàries Research Foundation- c/ Dr. Pujades 38- 08830- Sant Boi de Llobregat, Barcelona- Catalonia- Spain, Spain*
[5] *University of Clermont Auvergne, CHU Clermont-Ferrand-Department of Psychiatry- EA 7280- University of Clermont Auvergne- 58- Rue Montalembert- 63000., Clermont-Ferrand- France, France*
[6] *Chaim Sheba Medical Center, Psychiatry B- Chaim Sheba Medical Center- Ramat-Gan- Israel., Ramat-Gan- Israel, Israel*
[7] *sychiatric Pole- Sainte Marguerite, AP HM- Psychiatric Pole- Sainte Marguerite- Marseille- France, Marseille-France, France*
[8] *University of Zurich, Department of Psychiatry- Psychotherapy and Psychosomatics- Psychiatric Hospital- University of Zurich- Switzerland., Zurich- Switzerland, Switzerland*
[9] *University of Texas Health Science Center at San Antonio, Department of Psychiatry- University of Texas Health Science Center at San Antonio- San Antonio- TX- USA, San Antonio- TX- USA, USA*
[10] *Moscow Research Institute of Psychiatry, Department for Therapy of Mental Disorders- Moscow Research Institute of Psychiatry- Moscow- Russia., Moscow- Russia, Russia*
[11] *Institute of Psychiatry- Psychology & Neuroscience. King's College London., Centre for Affective Disorders- Department of Psychological Medicine- Institute of Psychiatry-Psychology & Neuroscience- King's College London- London-UK., London- UK., Unit*
[12] *University of Pisa, Department of Experimental and Clinical Medicine- Section of Psychiatry- University of Pisa- Via Roma 67- 56100- Pisa- Italy., Pisa- Italy, Italy*

Background: Major depression (MDE) is a clinical syndrome occuring in approximately one out of six adults over a life-time. This syndromal transdiagnostic nosographic construct bears more than 1400 combinations of symptoms which may fulfil a diagnosis of MDE [1], and straddles Major Depressive Disorder (MDD) and Bipolar Disorder (BD). Despite cross-sectional similarities, these two conditions show differences in their neurobiological underpinnings, clinical presentation, course of illness and, ultimately, functional outcome. Thus, prognostic and treatment implications warrant a differentiation between these two disorders [2]. Network approaches to psychopathology support that mental disorders arise from the interplay between symptoms in a network structure. Network analysis is a novel and alternative approach that outlines symptoms interactions in psychopathological networks and which may lead to significant improvements in research on and treatment of psychopathology [3]. Major depression has been analyzed using network analysis, and exposed as a complex dynamic system in which symptoms are directly connected to one another in a network structure. According to this approach, individuals more vulnerable to MDE have been defined as those with strong connections between symptoms: when pushed by external forces to the system (such as stress), they are more likely to end up in a depressed state [4]. The Bipolar Disorders: Improving Diagnosis, Guidance and Education (BRIDGE)-II-MIX study was a multicenter, multinational, non-interventional, cross-sectional study aimed at the clinical characterization of mixed features in a large population of acutely depressed patients [5].

Aim: To characterize symptom networks in acutely depressed MDD and BD patients and to verify possible differences in psychopathological networks across the two subgroups.

Methods: From a total of 2811 individuals with MDE from the BRIDGE-II-MIX study, we analyzed 7 DSM-IV-TR criteria for MDE and 14 researched based domain criteria for mixed features (RBDC) in a sample of 2758 acutely depressed MDD-BD patients. A total of 53 patients were excluded due to missing in at least one of the symptoms variables used as nodes for the network analysis. The global network was described in terms of symptom thresholds, i.e. the independent disposition for a symptom to be present, and symptom centrality. Differences in endorsement rates for all 24 symptoms across subgroups were assessed by chi-squared tests using Bonferroni corrections. Similarities in endorsement rates were examined by Spearman rank-order correlations. Differences in symptom network