with decreased BDNF levels being associated with the emergence of depressive symptoms. More recent studies have reported that the precursor protein – proBDNF – might also be involved in the pathogenesis of depression since both particles are biologically active and elicit opposing effects: mature BDNF promotes the proliferation of neurons and synaptogenesis, while proBDNF evokes neuronal death. The BDNF/proBDNF ratio has been suggested as a possible biomarker of depression state and treatment response among adults with depression. However, no study has analyzed BDNF/proBDNF serum ratio levels in adolescent depressed patients.

Objectives: We aimed to verify the changes in serum BDNF/proBDNF ratio levels during the course of treatment in adolescents with depression in relation to healthy control. We also aimed to investigate whether this parameter could predict the antidepressant treatment outcome.

Methods: Thirty female inpatients, aged 11-17, diagnosed with a first-lifetime depressive episode were assessed at two time-points: before (t0) and after (t1) the minimum six-week period of the first-line antidepressant treatment and compared with thirty age-matched healthy girls. The assessment at t0 and t1 involved the analysis of BDNF and proBDNF serum levels (ELISA method) and clinical symptoms evaluation using standardized depressive symptoms scales: Children's Depression Inventory (CDI-2) and Hamilton Depression Rating Scale (HDRS). Patients with at least 50% symptom reduction in CDI-2 and HDRS or HDRS<7 were classified as 'responders.' The control group underwent one-time BDNF and proBDNF evaluation. The BDNF/proBDNF ratio has been calculated.

Results: The BDNF/proBDNF serum ratio did not significantly differ between the studied and control groups. We proved no significant differences in BDNF/proBDNF serum ratio before and after the antidepressant treatment, regardless of the treatment outcome. However, responders had a significantly higher pretreatment BDNF/proBDNF ratio when compared with non-responders (Figure 1). The ROC analysis revealed that the BDNF/proBDNF ratio at t0 could predict the remission status at t1 with a sensitivity of 66.67% and a specificity of 81.25% (Figure 2).

Image 1:

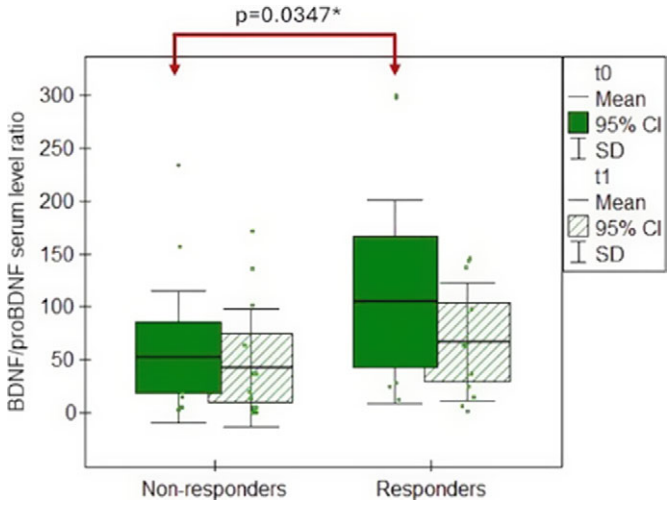
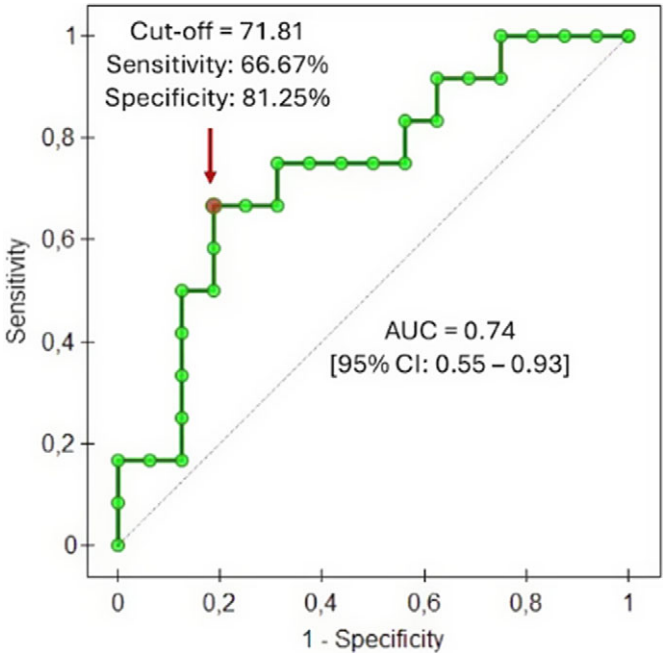


Image 2:



Conclusions: Pretreatment BDNF/proBDNF ratio could be considered a possible biomarker predictive of antidepressant treatment response in adolescent girls.

Disclosure of Interest: None Declared

Comorbidity/Dual Pathologies

EPP018

Genetic overlap of severe psychiatric disorders with lung function and asthma suggests shared biological mechanisms

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Introduction: Severe psychiatric disorders, including schizophrenia (SCZ), bipolar disorder (BIP) and anorexia nervosa (AN), are frequently comorbid with lung function decline and asthma. Despite considerable heritability, the genetic relationships between severe psychiatric and respiratory comorbidities are inconclusive.

Objectives: We aimed to thoroughly investigate the shared genetic architecture between three severe psychiatric disorders (SCZ, BIP and AN) and lung function (forced expiratory volume/forced vital capacity ratio) or doctor-diagnosed asthma based on available genome-wide association studies.

Methods: We performed linkage disequilibrium score regression analyses (LDSC) and MiXeR to quantify the genetic overlap. A conditional/conjunctional false discovery rate (cond/conjFDR) approach was employed to detect shared genomic loci. Functional annotations, gene mapping and gene-based enrichment analyses were adopted to explore shared biological mechanisms. Web-based cell-type-specific enrichment analysis (WebCSEA) was employed to identify the cell types enriched for shared genes across tissues. Transcriptome analyses were conducted via S-PrediXcan to prioritize biologically plausible shared genes in relevant tissues.
Results: Despite weak or null genetic correlations identified by LDSC, MiXeR analyses demonstrated extensive moderate polygenic overlap (~400 to 800 shared variants) across all pairs of psychiatric and respiratory phenotypes. The cond/conjFDR approach detected a total of 378 unique loci jointly associated with severe psychiatric disorders and lung function or asthma, harboring a mix of concordant and antagonistic variants. Gene-based enrichment analyses applied to the 4,105 genes mapped to shared loci highlighted cell types including type II pneumocytes and macrophages in lung and monocytes in blood as well as biological processes involving the interferon (IFN) JAK-STAT pathway and natural killer cell activation, suggesting common immune mechanisms. Furthermore, when stratified by respiratory outcome, genes shared with asthma were enriched for immunity-related pathways, whereas genes shared with lung were enriched for non-immune mechanisms, indicating divergent shared etiology. A total of 22 shared genes identified by conjFDR approach were prioritized as biologically plausible in transcriptome analyses.
Conclusions: This study reveals the complicated shared genetic etiology between severe psychiatric disorders and lung function or asthma and implicates overlapping immune and non-immune mechanisms. Our findings suggest that individuals with severe psychiatric disorders should be screened for lung function decline and asthma in clinical settings.

Disclosure of Interest: None Declared

EPP019

AI-based diagnosis of depression and cardiovascular disease comorbidity based on big data

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Introduction: There is strong clinical evidence that patients with depression have high probabilities to present a cardiovascular disease and vice versa. Thus, it is important to accurately identify these patients in order to provide the optimal management of the comorbid conditions.
Objectives: To identify patients who have depression and cardiovascular disease using social and molecular biomarkers which are routinely collected in the clinical practice.
Methods: Data from 502,379 participants in the UK Biobank were utilized in this work. A subset of the participants has a mental assessment using questionnaires about the presence of depression. CVD assessment was also available for the majority of the patients. In total, 126,033 participants had clinical assessment of both depression and CVD. From these, 8,925 patients had both comorbid conditions. An automated medical data curation tool described in a previous study was utilized to detect and mitigate data inconsistencies and elevate the input data integrity and usability. Hybrid boosting ensembles, including the XGBoost algorithm with a customized hybrid loss function was trained on the curated data, to reduce training and testing loss and to avoid overfitting effects. Dropout rates from deep learning theory were used in the hybrid loss function to further reduce biases during the decision-making process by controlling for the shape of the loss function. Random downsampling with replacement was also applied to match the control and target populations due to the increased class imbalance (ratio?) and with respect to the pre-defined set of confound factors. Additional classifiers including bagging classifiers were used for comparison purposes. The classification performance was assessed based on stratified 10-fold cross validation, where various metrics like the accuracy, sensitivity, specificity and area under the ROC curve scores were estimated. Advanced feature selection methods from coalition game theory, including the Shapley additive explanation (SHAP) exploratory analysis was utilized to identify predictors with positive or negative impact to have both the comorbid conditions These explanations were based on the classification outcomes from specific training and testing instances.
Results: The XGBoost classifier had the best performance among all tested classifiers. The results were 0.85, 0.88, 0.81 and 0.92 for the accuracy, sensitivity, specificity and AUC, respectively. The figure 1, presents the explainability analysis for the selected biomarkers. As shown, there are simple social questions, but also some blood biomarkers which can be used for the identification of the patients with both the comorbid conditions of depression and CVD.

Image 1: