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Unsupervised neurobiology-driven stratification of clinical heterogeneity in depression

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Introduction: One of the main obstacles in providing effective treatments for major depressive disorder (MDD) is clinical heterogeneity, whose neurobiological correlates are not clearly defined. A biologically meaningful stratification of depressed patients is needed to promote tailored diagnostic procedures.

Objectives: Using structural data, we performed an unsupervised clustering to define clinically meaningful clusters of depressed patients.

Methods: T1-weighted and diffusion tensor images were obtained from 102 MDD patients. In 64 patients, clinical symptoms, number of stressful life events, severity and exposure to adverse childhood experiences were evaluated using the Beck Depression Inventory (BDI), Schedule of Recent Experiences (SRE), Risky Family Questionnaire (RFQ), and Childhood Trauma Questionnaire (CTQ). Clustering analyses were performed with extracted tract-based fractional anisotropy (TBSS, FSL), cortical thickness, surface area, and regional measures of grey matter volumes (CAT12). Gaussian mixture model was implemented for clustering, considering Support Vector Machine (SVM) as classifier. A 10x2 repeated cross-validation with grid search was performed for hyperparameters tuning and clusters' stability. The optimal number of clusters was determined by normalized stability, Akaike and Bayesian information criterion. Analyses were adjusted for total intracranial volume, age, and sex. The clinical relevance of the identified clusters was assessed through MANOVA, considering domains of clinical scales as dependent variables and clusters' labels as fixed factors. Discriminant analysis was subsequently performed to assess the discriminative power of these variables.

Results: Cross-validated clustering approach identified 2 highly stable clusters (normalized stability=0.316, AIC=-80292.48, BIC=351329.16). MANOVA showed a significant between-clusters difference in clinical scales scores (p=0.038). Discriminant analysis distinguished the two clusters with an accuracy of 78.1%, with BDI behavioural and CTQ minimisation/denial domains showing the highest discriminant values (0.325 and 0.313).

Conclusions: Our results defined two biologically informed clusters of MDD patients associated with childhood trauma and specific clinical profiles, which may assist in targeting effective interventions and treatments.

Disclosure of Interest: None Declared

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Structural neuroimaging differentiates between depressed bipolar disorder and major depressive disorder patients: a machine learning study

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Introduction: Depression is the predominant mood alteration in bipolar disorder (BD), leading to overlapping symptomatology with major depressive disorder (MDD). Consequently, in clinical assessment, almost 60% of BD patients are misdiagnosed as affected by MDD. This calls for the creation of a framework for the differentiation of BD and MDD patients based on reliable biomarkers. Since machine learning (ML) enables to make predictions at the single-subject level, it appears to be particularly suitable for this task.

Objectives: We implemented a ML pipeline for the differentiation between depressed BD and MDD patients based on structural neuroimaging features.

Methods: Diffusion tensor imaging (DTI) and T1-weighted magnetic resonance imaging (MRI) data were acquired for 282 depressed BD (n=180) and MDD (n=102) patients. Axial (AD), radial (RD), mean (MD) diffusivity, and fractional anisotropy (FA) maps were extracted from DTI images, and voxel-based morphometry (VBM) measures were obtained from T1-weighted images. Each feature was entered separately into a 5-fold nested cross-validated ML pipeline differentiating between BD and MDD patients, comprising: confound regression for nuisance variables removal (i.e., age and sex), feature standardization, principal component analysis, and an elastic-net penalized regression. The models underwent 5000 random permutations as a test for significance, and the McNemar's test was used to assess whether there was any significant difference between the models (significance threshold was set to $p<0.05$).

Results: The performance of the models and the results of the permutation tests are summarized in Table 1. McNemar's test showed that the AD-, RD-, MD-, and FA-based models did not differ between each other and were significantly different from the VBM.

Table 1. Models' performance and p-value at 5000 permutation test.

Feature	Overall accuracy	MDD specifictiy	BD sensitivity	p-value
VBM	0.61	0.38	0.74	0.058
AD	0.78	0.65	0.86	<0.001
FA	0.79	0.61	0.89	<0.001
MD	0.79	0.63	0.88	<0.001
RD	0.79	0.63	0.88	<0.001