EPP1004

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

EPP1005

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

Conclusions: In conclusion, our models differentiated between BD and MDD patients at the single-subject level with good accuracy using structural MRI data. Notably, the models based on white matter integrity measures relying on true information, rather than chance.

Disclosure of Interest: None Declared

EPP1006

Different patterns of frontal and temporoparietal activities related to distinct inhibitory functions in adhd

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Introduction: Inhibition is a core component of executive functions but is not a unitary construct. Instead, different inhibitory processes have specific behavioral effects and neural bases. Three important inhibitory functions explored by the literature are 1) interference control (i.e., inhibition of distractive information); 2) inhibition of prepotent responses and 3) inhibition of ongoing responses. These functions were described in the self-regulation theory as the possible main impairment in attention-deficit hyperactivity disorder (ADHD) and since then they have shown an association with several psychiatric disorders.
Objectives: The current study investigated the neural bases of interference control, inhibition of prepotent responses, and inhibition of ongoing responses as they were assessed by a Stroop-matching/stop-signal task developed by our group.
Methods: The Stroop-matching/stop-signal employs different conditions to create the demands for each inhibition which allows the assessment of these functions using a single protocol. Brain activations were acquired using fNRIS in a block-design method. The concentration of oxygenated hemoglobin (HbO). The first level analysis of HbO signals used a general linear model (GLM) to estimate individual brain activations. The second level analysis was performed using a linear mixed model to generate brain activations at the group level. Alpha level = 0.05 and the false discovery rate was applied when necessary. The sample was composed of 25 young adults (mean age = 21.8, SD = 4.39).
Results: task Interference control showed activation in the left and right temporoparietal junction (TPJ), the right dorsolateral prefrontal cortex (DPLFC), and inferior frontal gyrus (IFG); inhibition of prepotent responses showed increased activity in the right IFG and left DLPFC; the suppression of ongoing responses showed a deactivation of the IFG and DLPFC bilaterally.
Conclusions: These results indicate that the three inhibitory functions assessed present distinct brain patterns of function. The lateralization role was evident in DLPFC and IFG activities and recruitment of parietal areas seems to be limited to interference control in this protocol. Also, the stop-signal demand led to the deactivation of areas associated with the resolution of the primary Stroop-matching task. This study elucidates the role of brain mechanisms associated with specific inhibitory processes that are impaired in psychiatric disorders such as ADHD.
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EPP1007

Alteration of plasma phospholipids distinguish schizophrenic patients from controls: A targeted metabolomics study

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Introduction: Schizophrenia (SCZ) is one of the most severe mental disorders. Several elements involved in pathogenesis have been characterized recently. However, tools for diagnosis and risk prediction are limited. Elucidation of the underlying genomic and molecular mechanisms of SCA remains a challenge.
Objectives: In this study, we aimed to identify plasma biomarkers for SCZ using targeted metabolomics.
Methods: All enrolled patients were drug-free for at least 3 months prior to admission. Plasma from 31 SCZ patients and 70 matched controls were analyzed using the LC/MS- Api 4000 QTrap Sciex. A total of 188 targeted metabolites, including 21 amino acids, 21 biogenic amines and 145 lipids or lipid-related metabolites were analyzed. All data modeling and analysis is done using MetaboAnalyst 5.0
Results: There was no significant difference in the studied groups regarding BMI. Plasma Triglycerides, LDL-C, total proteins levels were significantly decreased in SCZ compared to controls. Heatmap identified 2 clusters with 25 significantly differentially expressed metabolites (FDR <0.05) between the drug-naïve group and the matched controls. The OPLS-DA score plot showed that the groups are clearly separated according to plasma phospholipids concentrations. Among these differential metabolites, the expression level of very long chain Phosphatidylcholines (PC 36 – PC p42) and acylcarnitines were significantly decreased in SCZ compared to controls, whereas sphingomyelin (SM) and lysoPC were significantly lower in drug-naive patients.
Conclusions: In this study, we found that plasma phospholipids were significantly dysregulated in the SCZ patients and could be a promising pathway to explore SCZ.

Disclosure of Interest: None Declared