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MOVING BEYOND CLINICAL APPROACHES: MACHINE LEARNING ON NEUROIMAGING AND COGNITIVE FEATURES FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN UNIPOLAR AND BIPOLAR DEPRESSION

E. Serra [1], F. Calesella [1,2], F. Colombo [1,2], B. Bravi [1,2], L. Fortaner-Uyà [1,2], C. Monopoli [1], S. Poletti [1,2], I. Bollentini [1], F. Benedetti [1,2], B. Vai [1,2]. [1] *IRCCS San Raffaele Research Institute, Psychiatry and Clinical Psychobiology Unit-Division of Neuroscience, Milan, Italy;* [2] *Vita-Salute San Raffaele University, Department of Psychology, Milan, Italy*

Background: Depression is a hallmark of bipolar disorder (BD) and is often the initial symptom leading patients to seek clinical support [1]. Consequently, BD is initially misdiagnosed as major depressive disorder (MDD) in 60% of cases, resulting in tortuous treatment journeys and suboptimal clinical outcomes [2]. Hence, there is a necessity to identify unique and differential markers for depression in BD compared to MDD which can be harnessed to improve diagnostic accuracy. Notably, structural brain alterations are well-characterised and distinctively related to BD and MDD pathophysiologies [3]. Furthermore, cognitive dysfunctions are observed in both conditions, yet their extent and nature may be idiosyncratic [4]. Development of a predictive framework based on such markers may represent the solution to misdiagnosis. In this context, a machine learning (ML) approach is especially promising, as it enables effective management of high-dimensional data while allowing for individual-level predictions.
Aim: The current study investigates the use of ML frameworks for accurate differentiation between BD and MDD patients based on measures of structural brain architecture and cognitive dysfunction.
Methods: Diffusion tensor imaging (DTI) and T1-weighted MRI data were acquired from 141 patients with depression (BD: n=71; MDD: n=70). Region of Interest based values were extracted for fractional anisotropy (FA) from DTI images, and for voxel-based morphometry (VBM) and cortical thickness measures from T1 volumes. Cognitive dysfunction was measured through Brief Assessment of Cognition in Schizophrenia (BACS). All predictors were standardised and entered in a support vector machine (SVM) for classification in a 5-fold nested cross-validation. Confounding effects of age, sex, age by sex and age squared were regressed out from each feature within the cross-validation scheme. Six models were estimated: four entering each predictor separately, one based on neuroimaging features only, and one concatenating all features. Models underwent a 5000-permutation test to assess statistical significance ($p<0.05/6=0.008$).
Results: Values of classification performance and significance are summarised in Table 1 for each model. Notably, the only significant and most predictive model was that which concatenated both structural neuroimaging and cognitive measures.

Table 1Performance of SVM models in categorising BD and MDD patients.

Model	Accuracy (%)	Specificity (%)	Sensitivity (%)	PPV (%)	NPV (%)	P-Value
FA	61	63	59	62	60	0.013
VBM	53	61	45	54	52	0.166
Cortical thickness	57	46	68	56	58	0.084
BACS	56	59	54	57	55	0.091
Neuroimaging-only	58	53	63	58	59	0.053
Concatenated	62	70	53	60	64	0.004*

Abbreviations. PPV: Positive Predictive Value; NPV: Negative Predictive Value; *p<0.008.

Conclusion: The present study suggests structural alterations and cognitive dysfunction may be harnessed to efficiently differentiate between depressed patients diagnosed with BD and MDD. Interestingly, along with single-feature models, the neuroimaging-only model was not significantly more predictive than chance level differentiation. Conversely, the addition of cognitive dysfunction as a predictor allowed for classification to become significantly different from null model distribution, suggesting reliance on true information within the data rather than chance. This suggests that the combination of anatomical and cognitive characteristics is instrumental to differentiate between bipolar and unipolar depression.

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COGNITIVE DISTORTIONS AND STRUCTURAL NEUROIMAGING DATA PREDICT DEPRESSION SEVERITY IN UNIPOLAR AND BIPOLAR DEPRESSION: A MACHINE LEARNING STUDY

S. Perziani [1], F. Colombo [1,2], F. Calesella [1,2], L. Fortaner-Uyà [1,2], C. Monopoli [1], B. Bravi [1,2], S. Poletti [1,2], I. Bollettini [1], F. Benedetti [1,2], B. Vai [1,2]. [1] *IRCCS San Raffaele Hospital, Psychiatry and Clinical Psychobiology Unit- Division of Neuroscience, Milan, Italy;* [2] *University Vita-Salute San Raffaele, Department of Psychology, Milan, Italy*

Background: Cognitive distortions are considered pivotal to depressive symptomatology, representing a common feature of both major depression (MDD) and bipolar disorder (BD) [1]. Previous studies have shown evidence for the reliability of structural alterations as possible biomarkers of depression severity [2,3], however, it is still unclear whether the integration of neurobiological markers with cognitive distortions could boost the prediction of depression severity.
Aims: Operating a transdiagnostic approach, this study aims to provide a predictive model of depression severity by combining cognitive distortions and structural neuroimaging data using machine learning (ML).
Methods: Diffusion tensor imaging (DTI) and T1-weighted MRI data were acquired from 147 patients (MDD=55, BD=92). Depression severity was rated with the Beck Depression Inventory-Short Form and a standardised cut-off was used to identify patients with moderate (n=78) and severe (n=69) depression [4].