pallidum ($p < .05$, corrected).

Conclusions: Our findings demonstrated that SSD patients exhibit significant volumetric and surface-based morphological alterations in the BG, particularly in the putamen, pallidum, and accumbens. Notably, surface-based analyses identified localized shape deformations that were associated with NSS severity, suggesting that regional morphological changes of the BG, rather than global volumetric differences, may underlie sensorimotor dysfunction. These results underscore the role of BG abnormalities in the neurobiological basis of NSS and highlight their potential as structural markers of disease-related sensorimotor impairment in SSD.

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STAGE-SPECIFIC MOLECULAR ALTERATIONS IN BIPOLAR DISORDER: DNA METHYLATION, GENE EXPRESSION, AND MIRNA PROFILES

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Introduction: Despite significant advances in the understanding of bipolar disorder (BD), there remains a critical need for reliable biomarkers to improve diagnostic accuracy, predict progression, and optimize treatment strategies. Currently, the diagnosis is primarily based on clinical assessment, which can lead to delayed treatment and suboptimal outcomes. This subjectivity contributes to frequent misdiagnosis and compromises early intervention efforts. The development of a more refined staging model for BD, supported by objective markers, is essential for addressing the heterogeneity of the disorder and facilitating personalised treatment strategies [1].

Aim: In this study, we present data derived from a well-characterised cohort comprising 92 bipolar patients, stratified into four different stages (stage 1/2/3/4), as well as 39 healthy controls and 8 first-degree relatives of bipolar patients without a diagnosis of BD. This study aimed to explore a comprehensive biomarker-based staging approach that could contribute to a more objective classification of BD.

Methods: Patients with BD and healthy controls were recruited from three psychiatric centres. Sociodemographic and clinical features, including the stage of the disorder, were collected. Genomic DNA and total RNA were obtained from peripheral blood mononuclear cells isolated from the whole blood of BD patients and healthy controls, whereas saliva was used to isolate exosomes, from which miRNAs were subsequently purified. The relative abundance of BDNF mRNA was assessed by real-time quantitative polymerase chain reaction; specific CpG sites DNA methylation at gene promoters was evaluated using Pyrosequencing; genome-wide DNA methylation analysis was performed by RRBS sequencing; miRNA expression profiles was analysed using whole miRNome arrays. Statistical analysis was performed using Graph Pad Prism 9.1.0 and R software.

Results: In blood samples, we observed significant alterations in BDNF gene expression (Mann-Whitney test, $p = 0.0223$), with notable differences between males and females across stages, and consistent changes in the percentage of DNA methylation at BDNF gene promoter (CTRL mean value: 8,140% ± 0,9643, BD stage 1 mean value: 5,179% ± 0,5204, BD stage 2 mean value: 8,267% ± 1,019, BD stage 3 mean value: 9,121% ± 1,217, BD stage 4 mean value: 4,846% ± 0,3098). Genome-wide DNA methylation analysis from saliva samples identified 95 differentially methylated genes between controls and BD patients, with 11 genes previously associated with mental health conditions and 3 specifically linked to BD through epigenetic regulation. Additionally, miRNA profiling detected 99 differentially regulated miRNAs in BD patients compared to controls using the ΔΔCt method [2]. Network analysis, performed using R software, revealed several miRNAs with high relevance scores targeting genes implicated in BD pathophysiology, including GAD1, DGKH, GABRA1, and CLOCK.

Conclusions: These findings indicate stage-specific epigenetic modifications and changes in gene expression that may serve as potential biomarkers of BD progression and response to treatment. This integrative approach, combining refined clinical staging with molecular profiling, provides novel insights into the basis of BD and may inform more personalised therapeutic strategies for this complex and heterogeneous disorder.

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Conflict of interest

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PERIPHERAL METABOLIC SIGNATURES IN PATIENTS WITH NEUROPSYCHIATRIC LONG COVID SYNDROME

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Neuropsychiatric symptoms, such as fatigue, cognitive impairment (e.g. concentrations and memory deficits) and depressed mood belong to the most common symptoms that evoke severe mental suffering for affected individuals [1]. Recent studies have demonstrated structural brain changes and highlighted the importance of neuroinflammation in the development of cognitive deficits as seen in long COVID patients [2]. However, to the best of our knowledge, a systematic analysis of peripheral metabolomic profiles in a patient cohort with neuropsychiatric symptoms, and an analysis of the molecular and metabolomic correlates of neuropsychiatric symptoms, has not yet been conducted. Therefore, we aimed to investigate systemic alterations in peripheral plasma metabolome profiles in patients with neuropsychiatric long COVID syndrome ("PC") compared to healthy survivors of SARS-CoV-2 virus infection ("HC_S") and healthy never-infected controls ("HC_N"). To this end, we used targeted mass spectrometry-based metabolomics to measure between-group differences in plasma concentrations of ~630 metabolite and lipid molecules. Furthermore, we aimed to investigate potential associations of those metabolites that changed between the three experimental cohorts with clinical symptom severity of depressive mood, cognitive deficits and memory deficits. Finally, we wanted to investigate potential associations of those metabolites that changed between cohorts with differences in cortical thickness in multiple brain regions. We found that patients with long COVID show subtle peripheral alterations in lipid species such as triacylglycerides and acylcarnitines, metabolites that may indicate potential disturbances in fatty acid metabolism and subsequently mitochondrial energy production – as it has been shown in ME/CFS patients [3, 4] – that might