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Metabolomic study of patients with bipolar disorder through ¹H Nuclear Magnetic Resonance (¹H NMR).

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Abstract

This study was based on the front of the significance and prevalence of bipolar disorder (BD) (1 - 3% of global population¹) and the uncountable damages that it can bring to the patients, to their familiars, and to the society. Therefore, the objective of this research was to identify key metabolites that can act as biomarkers for this psychopathology, through NMR blood serum analyses of healthy individuals (Control Group) and patients with BD in combination with chemometrics. We have used Principal Component Analysis (PCA) and Partial Least Squares Discriminant Analysis (PLS-DA) as to separate these two groups. Metabolomics data banks were used for interpretation of our findings and interpretation of 2D NMR spectra. The results point to seven key metabolites as possible biomarkers (one of the control group and the rest of the patients with BD); these are N-acetyl-L-alanine (healthy group), N-acetyl-L-phenylalanine, α-ketoisovaleric acid, N-acetyl aspartyl glutamic acid, lipoamide, α-ketoglutaric acid and L-glutamine. By virtue of this, it can be concluded that the strategy applied presents a potential tool for diagnosis/investigation of patients with BD and the molecular pathways involved in this psychopathology.

Key words:

Bipolar Disorder, Metabolomics, NMR and Biomarkers.

Introduction

BD is a mental illness that affects around 1 – 3% of global population¹. The early diagnosis is extremely important for the accuracy of treatment. However, usually, it happens later, when the patient already passed by the inadequate treatment². So, the goal of this study is to reveal key metabolites that can be possible biomarkers for the BD. Thereunto, it was collected blood serum samples of healthy individuals and of patients with BD and they were mixed with deuterated water and submitted to ¹H NMR analysis. After the data were obtained and chemometrics analyses using PCA and PLS-DA methods were performed. Moreover, we acquired 2D spectra, and to characterize them, metabolomics data banks were consulted.

Results and Discussion

Our results were previously published in the paper "¹H-NMR, 1H-NMR T2-edited, and 2D-NMR in bipolar disorder metabolic profiling³", where it was possible to observe changes among ¹H NMR spectra of the two groups³. The differences became more evident in the region of 1.00 – 4.40 ppm (Image 1a).

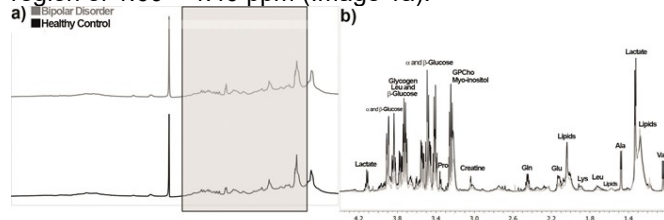


Image 1: 1a NMR spectra of patients with BD (grey) and Healthy control (black); 1b amplified NMR regions from 1.00 to 4.40 ppm. Furthermore, through T2-edited spectra, it was possible to characterize molecules and attribute peaks in the spectra (Image 1b). From these findings and chemometrics analyses, and the loading plots, the most significant NMR data in 1.00 to 4.40 ppm (Image 2c) where picked.

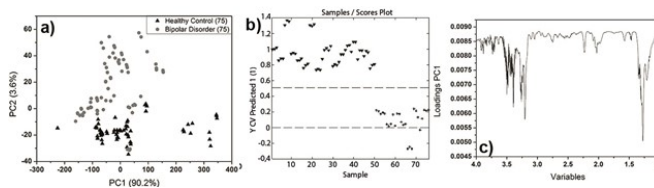


Image 2: 2a PCA 2b PLS-DA and 2c loading plot.

And to prove and let more specific the characterization of the metabolites found, 2D NMR Spectra of some sample of two groups (Image 3) were recorded and analyzed.

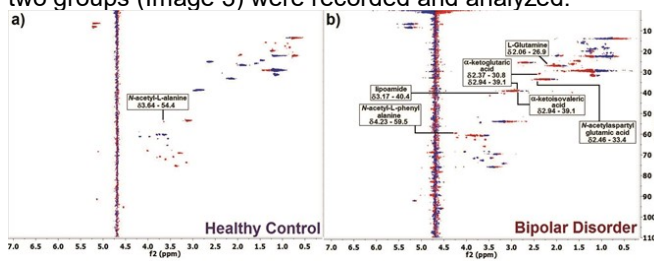


Image 3: 2D spectra 3a healthy control 3b BD patients.

Seven key metabolites were identified. Six of them were identified in blood serum sample of patients with BD, and just one in the sample of the healthy individual. They are: N-acetyl-L-alanine (healthy group), N-acetyl-L-phenylalanine, α-ketoisovaleric acid, N-Acetyl aspartyl glutamic acid, lipoamide, α-ketoglutaric acid and L-glutamine.

Conclusions

It can be concluded that the strategy applied has a potential as a tool for diagnosis/investigation of patients with BD and the molecular pathways involved in this psychopathology.

Acknowledgement



¹Goodwin FK, Jamison KR. Manic-depressive illness: bipolar disorders and recurrent depression. 2nd ed. New York: Oxford University Press; 2007.
²Phillips ML, Kupfer DJ. Bipolar disorder diagnosis: challenges and future directions. Lancet. 2013;381:1663–71.
³Sethi S, Pedrini M, Rizzo LB et al. 1H-NMR, 1H-NMR T2-edited, and 2D-NMR in bipolar disorder metabolic profiling. Int J Bipolar Disord. 2017 Dec 5(1):23.