

NMR metabolomics as diagnosis tool for schizophrenia

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Abstract

An organism's metabolic profile changes every day and even every hour. The development of advanced high resolution non destructive techniques, such as, nuclear magnetic resonance (NMR) allowed the research on how and when this profile changes and, more important, how they can be related with diseases by indentifying which molecules are associated for each symptom. Thus NMR metabolomics started to show potential for becoming a diagnosis tool. With NMR metabolomics and chemometrics we observed that it is possible to have evidences if someone is healthy or if is a schizophrenic person.

Key words:

Metabolomics, Schizophrenia, Diagnosis.

Introduction

The metabolome of an organism is a set of metabolites which are tiny molecules that play an important role in the cell activities or may be products of some protein synthesis. The metabolome changes its composition along the day and shows different profiles whether an organism is healthy or not. With the development of advanced techniques (e.g. NMR) that provides high-resolution non-destructive analyses, it is now possible to investigate how metabolome changes.¹

Results and Discussion

Our research is based on NMR analyses of blood serum samples from healthy people (control) and from those who demonstrated schizophrenia (SCZ) symptoms. The spectra were processed with a spreadsheet software and then analyzed with chemometrics techniques such as PCA and PLS-DA. The blood samples were collected using vacutainers with anticoagulant, between 8-10 h AM, centrifuged, and the supernatant, which is the blood serum, was kept at -80°C by the maximum period of 2 weeks. In a micro tube, 500 μL of deuterium oxide was mixed with the same amount of serum sample, and placed into a 5 mm NMR tube. Each sample was analyzed in triplicate, using a Bruker Avance III 600 MHz spectrometer, and analyses were done at 25°C .

The differences between the spectra (Figure 1) of healthy, which was used as control group, and SCZ people is observed in two NMR spectral regions, from 1.00 - 4.40 ppm and from 7.50 - 8.00 ppm. These regions were used for chemometrics analyses.

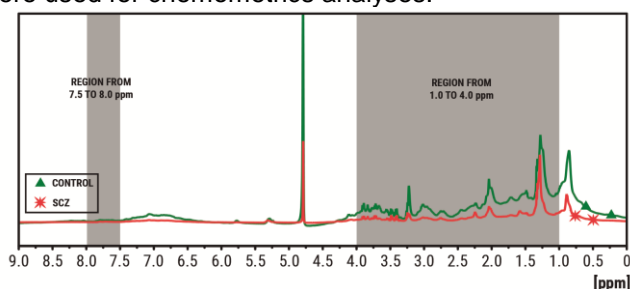


Figure 1. Typical ^1H NMR spectra of blood serum samples from healthy control, depicted in green, and SCZ, depicted in red. The regions used in chemometrics are accented with the grey shade.

^1H NMR chemical shifts from 7.50 to 8.00 ppm correspond to aromatic compounds and the other, 1.00 to 4.40 ppm to aliphatic compounds, amines and alcohols.

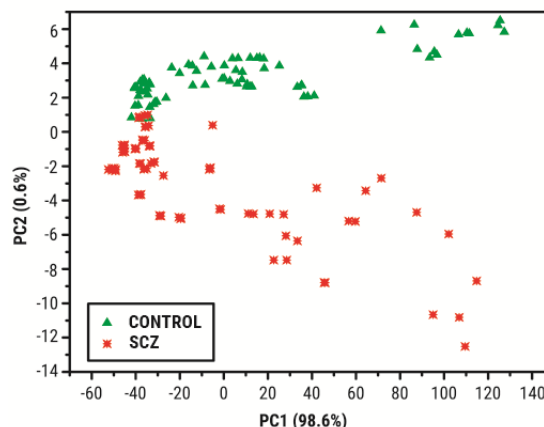


Figure 2. PCA-score graph using 25 samples of SCZ (red squares) and 24 samples of control group (green triangles) in triplicate, obtained for the NMR spectral region of 7.50 to 8.00 ppm.

The separation of the groups may be related to abnormalities of some neurotransmitters in SCZ patients, like dopamine and glutamate.²

Conclusions

PCA and PLS-DA analyses showed that the two groups can be differentiated with the information provided by the ^1H NMR spectra, suggesting that it can be a reliable diagnosis essay or, at least, a powerful aid to enhance the traditional method. The method should be repeated with a greater number of samples to minimize the effects of artifact signals, outliers and some other experimental errors.

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¹ Dettmer, K.; Aronov, P. A.; Hammock, B. D. *Mass Spectrom. Rev. Mass Spectrometry Reviews* 2006, 26 (1), 51–78.

² Laruelle, M.; Kegeles, L. S.; Abi-Dargham, A. *Annals of the New York Academy of Sciences* 2003, 1003 (1), 138–158.