DOI: 10.20396/revpibic2720192835

METABOLOMIC PROFILES OF PATIENTS WITH ISCHEMIC STROKE: SEARCHING FOR BIOMARKERS

Douglas C. Rosa*, Amanda Donatti, Fabiana S. Oliveira, Alexandre B. Godoi, Amanda Canto, Alessandro Sousa, Wagner. M. Avelar, Melissa Quintero, Ljubica Tasic, Iscia Lopes-Cendes.

Abstract

Ischemic stroke (IS) is one of the most common causes of mortality worldwide and represents 80% of all stroke cases. Previous studies have shown that some metabolites can be markers of oxidative injury to vascular endothelial cells and neuromodulation after brain ischemia. Biomarkers are small molecules that are dysregulated during diseases and that can be used to improve diagnosis and to determine prognosis, including responses to treatment. This study aims to identify if there are specific metabolites in the plasma of twenty patients with large vessels IS at the acute stage (less than 24 h after the event); twenty patients with large vessels IS at the chronic stage (more than 3 months after the acure event); twenty asymptomatic patients with severe internal carotid artery stenosis; and twenty healthy individuals. This last group is composed of individuals over fifty years old, who do not present internal carotid artery stenosis, who had no stroke and no first-degree relatives with stroke. Currently, we have evaluated plasma samples of 21 individuals, using proton Nuclear Magnetic Resonance (^{1}H NMR). The plasma samples were diluted in deutered water and the ^{1}H NMR spectra were recorded under the same conditions in a 600 MHz spectrometer.

Key words:

Stroke, Metabolomics, ^{1}H NMR.

Introduction

Stroke is caused by a blockage of the blood flow into the brain, resulting in neurological deficits [1]. Ischemic stroke (IS) is the most prevalent type, as it affects almost 85% of all stroke patients [2]. Atherosclerosis of large vessels is one of the most frequent subtypes of IS and it is mainly caused by an obstruction of large arteries due to thrombi formation derived from atherosclerotic plaques [1; 3]. The effects of ischemia on the neural tissue worsens with the increase of the injured area, while tissue recoveries strategies, as vase recanalization, have a pivotal role to avoid the increase of ischemic events at the penumbra and to prevent further neural injuries [4]. Despite all clinical knowledge, there are no biomarkers to determine whether a given patient will follow to the recanalization process, thus leading to clinical improvement, or he/she will get worse. One of the best ways to identify molecules present in a complex biological sample is the application of proton nuclear magnetic resonance (^{1}H NMR) in conjunction with the use of references in a databank and specific statistical strategies [5; 6]. Therefore, the present study aims to determine the metabolomic profiles of plasma samples from patients in the previous, acute and chronic stages of large vessels IS using ^{1}H NMR. The results of the metabolomic profiles will also be correlated with the NIH (National Institute of Health) stroke score variation, a measure of clinical evolution and prognosis.

Results and Discussion

To date, we have acquired ^{1}H NMR spectra of 21 samples (six from large vessels ischemic stroke at the acute stage, six from large vessels ischemic stroke at the chronic phase, five from healthy individuals and four from asymptomatic patients with severe internal carotid artery stenosis). So far, we have observed a qualitative difference between the intensities of the peaks of each group, and we aim to confirm these differences using the principal component analysis (PCA) and the partial least square discriminant analysis (PLS-DA).

Conclusions

Our preliminary results demonstrate that there are qualitative differences in the metabolomic profile of patients in different stages of IS when compared with control subjects. We believe that after completion, the present study may help to identify to key metabolic pathways involved in the pathophysiological process as well as recovery of IS in general and in large vessel disease.

Acknowledgement

This study is supported by CEPID-BRAINN, FAPESP; Faculty of Medical Sciences, University of Campinas (UNICAMP); and Institute of Chemistry, UNICAMP. DCR receives a scholarship from FAPESP (2019/00048-0). Comitê de Ética: 12112913.3.0000.5404/Parecer 257.020.

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