

# Metabolomic profiling of aqueous humor from glaucoma patients - The metabolomics in surgical ophthalmological patients (MISO) study

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Glaucoma is still a poorly understood disease with a clear need for new biomarkers to help in diagnosis and potentially offer new therapeutic targets. We aimed to determine if the metabolic profile of aqueous humor (AH) as determined by nuclear magnetic resonance (NMR) spectroscopy allows the distinction between primary open-angle glaucoma patients and control subjects, and to distinguish between high-tension (POAG) and normal-tension glaucoma (NTG) . We analysed the AH of patients with POAG, NTG and control subjects (n = 30/group) . <sup>1</sup>H NMR spectra were acquired using a 400 MHz spectrometer. Principle component analysis (PCA) , machine learning algorithms and descriptive statistics were applied to analyse the metabolic variance between groups, identify the spectral regions, and hereby potential metabolites that can act as biomarkers for glaucoma.

According to PCA, fourteen regions of the NMR spectra were significant in explaining the metabolic variance between the glaucoma and control groups, with no differences found between POAG and NTG groups. These regions were further used in building a classifier for separating glaucoma from control patients, which achieved an AUC of 0.93. Peak integration was performed on these regions and a statistical analysis, after false discovery rate correction and adjustment for the different perioperative topical drug regimen, revealed that five of them were significantly different between groups.

The glaucoma group showed a higher content in regions typical for betaine and taurine, possibly linked to neuroprotective mechanisms, and also a higher content in regions that are typical for glutamate, which can indicate damaged neurons and oxidative stress. These results show how aqueous humor metabolomics

based on NMR spectroscopy can distinguish glaucoma patients from controls with a high accuracy. Further studies are needed to validate these results in order to incorporate them in clinical practice.

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Exp Eye Res. 2020 Oct 1;201:108268.doi: 10.1016/j.exer.2020.108268. Online ahead of print.

PMID: 33011236