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^1H -NMR spectroscopy based metabolomic analysis has diagnostic potential in Idiopathic Intracranial Hypertension and sheds light on disease processes

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INTRODUCTION

Idiopathic intracranial hypertension (IIH)

- Characteristic raised intracranial pressure (ICP).
- Affects young, obese women causing severe headaches and 10% risk of blindness.⁽¹⁾
- 40% diagnostic error rate.⁽²⁾
- Pathophysiology is poorly understood. Recent evidence suggests metabolic disturbances may be present.⁽³⁾

AIMS

1. Are systemic metabolic disturbances evident in IIH?
2. Do metabolomic changes correlate with visual outcomes in IIH?
3. Does metabolomic profiling have diagnostic value in IIH?

METHODS

IIH patients*

Mean age 33.0±7.1y
Mean BMI 42.2±7.9
n = 84

Controls*

Mean age 36.6±8.5y
Mean BMI 43.7±5.0
n = 20

- Visual field perimetry → mean deviation measured (worse eye for each patient)
- CSF and serum samples collected
- Extracted with Chloroform + Methanol

- ^1H -NMR spectra acquired and baseline corrected using MetaboLab
- Untargeted metabolomic profiling of spectra using Chenomx NMR Suite
- Data normalisation and statistical analysis

*Matched for age, gender and BMI.

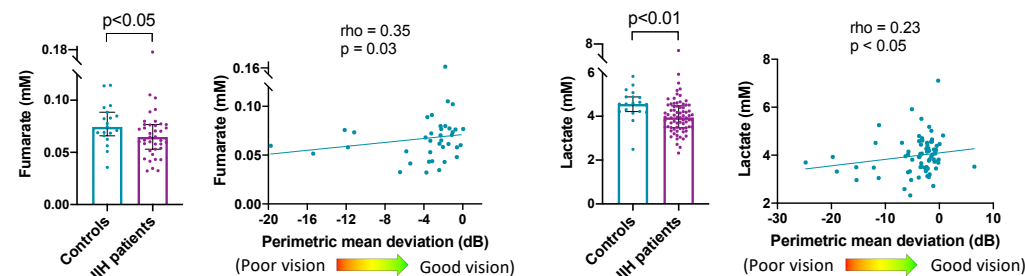
RESULTS

Systemic metabolic disturbances are evident in IIH

CEREBROSPINAL FLUID (CSF)

23 of 47 metabolites detected were significantly different between patients and controls

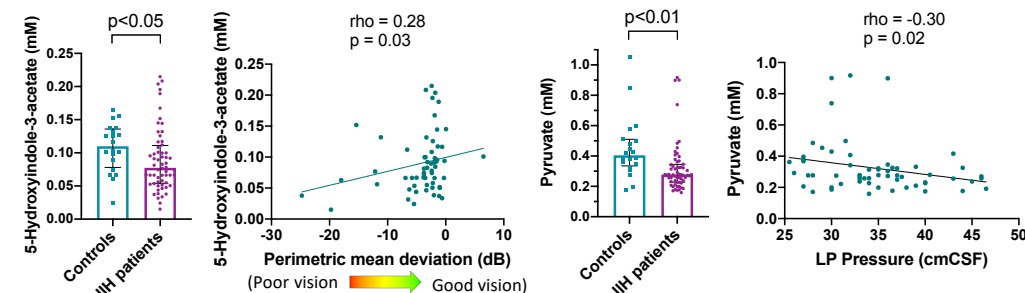
Figure 1. CSF Fumarate and Lactate correlated with perimetric mean deviation in IIH patients.



SERUM

12 of 45 metabolites detected were significantly different between patients and controls

Figure 2. Serum 5-Hydroxyindole-3-acetate correlated with perimetric mean deviation and Serum Pyruvate correlated with lumbar puncture (LP) pressure (surrogate marker of ICP) in IIH patients.



CSF and Serum metabolomic profiling have diagnostic value in IIH

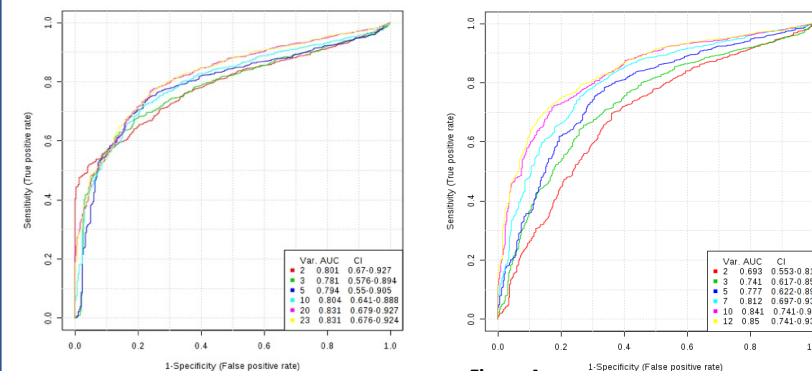


Figure 3

CSF

AUC of ROC curve produced using 23 differential CSF metabolites
0.83 (95% CI 0.68-0.92)

Figure 4

SERUM

AUC of ROC curve produced using 12 differential Serum metabolites
0.85 (95% CI 0.74-0.93)

Abbreviations: AUC; area under curve, ROC; receiver operating characteristic

CONCLUSIONS

- IIH patients have unique metabolite profiles, predominantly seen in CSF but also manifesting in serum. Thus, IIH is not merely a disease of the brain but a disease with significant global metabolic dysregulation.
- Individual metabolite levels correlate with visual parameters in IIH.
- Developing a serum based diagnostic tool for IIH could prevent the need for diagnostic lumbar punctures and reduce overdiagnosis rates.⁽²⁾

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