Increased systemic and adipose 11β-HSD1 activity in idiopathic intracranial hypertension

Background

Idiopathic intracranial hypertension (IIH) most often occurs in young women and is more often found in those with increased body weight. Recent studies have shown that IIH is more than a disease of the brain and eyes. People with IIH are insulin and leptin resistant and have fat programmed for making more fat (https://insight.jci.org/articles/view/145346). Also, people with IIH are at increased risk of cardiovascular disease and type 2 diabetes in IIH patients above and beyond that caused by weight alone (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6618853/?report=printable). Together this research suggests an underlying metabolic problem in people with IIH.

Several clinical studies in IIH have looked at glucocorticoids (GC's), a class of hormones that promote metabolic dysfunction when higher than normal. Reducing exposure to active GC's has been shown to be associated with improvement in IIH (https://academic.oup.com/jcem/article/95/12/5348/2835270?login=true) . This could suggest that people with IIH have abnormal GC metabolism, however it is unknown if this is true.

What was the aim of the study?

To investigate the above research further, we conducted very detailed analysis of GC metabolism in people with IIH. The results were recently published and the full text of this research is available at: https://eje.bioscientifica.com/view/journals/eje/187/2/EJE-22-0108.xml

How was the study performed?

The research contains 3 studies. The first study compares people with IIH to people without IIH where both groups were matched to be the same weight, age and sex. This means the results were not driven by weight or age, but other factors. In this first study, we show that people with active IIH have increased activity of the enzyme 11β-HSD1 (11β-hydroxysteroid dehydrogenase-1). This indicated an increased ability to generate metabolically active GCs. Indeed, people with IIH had increased levels of the metabolically active GC cortisol. There was no association between and GC measurements and raised brain pressure.

The second study used data from people with IIH who were enrolled in the IIH:WT (https://jamanetwork.com/journals/jamaneurology/fullarticle/2778650). Here we compared the effects of bariatric surgery against a community weight loss strategy on GC metabolism. We show that the weight loss caused by bariatric surgery reduces the activity of the enzyme 11β-HSD1. Reduction in 11-βHSD1 enzyme activity was associated with reduced ICP.

In the final study we demonstrated that the fat from people with IIH have increased activity of the enzyme 11β-HSD1 compared to individuals of the same age, sex and weight. This could explain the previous findings of IIH fat being prone to weight gain. GCs help fat store calories.

What were the overall findings of the research?

This research provides evidence that IIH is more than a disease of the eyes and brain. It is unknown if the altered GC metabolism has a role in brain pressure in IIH. However, these findings do suggest that fat tissue in IIH contributes to altered GC metabolism. More work needs to be done to understand the meaning of this for people with IIH and the disease.

Key points of the research

- The study demonstrates that in IIH, there is elevated 11β-HSD1 activity in excess to that mediated by obesity alone.
- Bariatric surgery to induce weight loss was associated with reductions in 11β-HSD1 activity and decreased ICP.
- Overall this shows that IIH is not just a disease of the eyes and brain, but is caused by altered metabolism in the body.