Nature Reviews Gastroenterology & Hepatology **12**, 488 (2015); published online 28 July 2015; doi:10.1038/nrgastro.2015.130

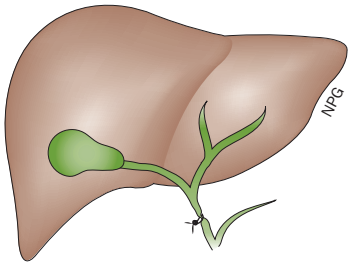
SURGERY

Bile diversion comparable to bariatric surgery in mice

Re-routing the flow of bile to the ileum results in physiological and metabolic improvements equivalent to those seen after Roux-en-Y gastric bypass (RYGB) surgery in a mouse model of obesity, according to new research published in *Nature Communications*.

Existing evidence showed that RYGB surgery is associated with increased levels of bile acids, and it is these bile acids that are thought to mediate some of the beneficial effects of bariatric surgery. "We devised a much simpler surgical procedure aimed at achieving similar elevations in plasma bile acids and examined the effects of such a procedure on changes in body weight and insulin sensitivity," explains author Naji Abumrad, testing this approach in a mouse model of diet-induced obesity (DIO; fed a high-fat diet).

In their procedure, the common bile duct was ligated proximal to the pancreatic duct and the gallbladder then attached to several sites along the gastrointestinal tract: the duodenum, jejunum or ileum. DIO mice underwent either of the bile diversion procedures or RYGB. Body weight, adiposity, glucose homeostasis and liver metabolism were monitored over an 8-week period.



Interestingly, only bile diversion to the ileum (4 cm proximal to the ileocaecal valve; termed the GB-IL procedure) led to metabolic improvements equal to those observed after RYGB, including weight loss and reduction in fat mass, as well as improvements in glucose tolerance, insulin sensitivity and hepatic steatosis. "Remarkably, in the GB-IL animals—which do not have any manipulation of their stomach or intestines—exhibit decreased food intake similar to the RYGB animals that suggests to us that bile acid elevations are acting or modifying some neuroendocrine mechanism(s) to promote satiety," adds Abumrad.

Crucially, serum levels of total bile acids increased with the GB-IL procedure by nearly tenfold, particularly driven by tauro-ω-muricholic acid and tauro-β-muricholic acid, the latter a potent farnesoid X receptor (FXR) antagonist. No major increases in total or individual bile acid levels were seen after RYGB.

Finally, the researchers found that hepatic FXR–FGF15 signalling and composition of the gut microbiota were altered after GB-IL. High-fat diets led to decreased microbial diversity in the mice, alongside changes in the abundance of certain phyla (such as decreased proportion of Bacteroidetes and increased Firmicutes); these gut microbiota changes were partially reversed after GB-IL.

More studies are planned to confirm the findings and identify the underlying mechanisms. "It is important to note that these findings cannot yet be translated to humans before more thorough examinations are carried out in larger animal models," says Abumrad, cautioning that, although this bile diversion procedure has all the benefits of RYGB without the surgical complexity, much progress needs to be made before we will see it in clinical practice.

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Original article Flynn, C. R. *et al.* Bile diversion to the distal small intestine has comparable metabolic benefits to bariatric surgery. *Nat. Commun.* **6**, 7715 (2015)