Role of butyrate in restoring satiety signaling in rodent model of high-fat (HF) diet-induced obesity

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Background
- The vagal afferent neural pathway communicates the presence of nutrients in the gut to the brain to induce satiety.
- However, chronic ingestion of a high-fat diet (HFD) blunts vagal afferent neuron (VAN) sensitivity to anorexigenic gut hormones, such as cholecystokinin (CCK), resulting in hyperphagia and obesity.
- In a previous investigation, pre-biotics attenuated the deleterious effects of a HFD and increased butyrate concentration in the gut lumen.
- Butyrate, a short-chain fatty acid produced in the gastrointestinal (GI) tract by the fermentation of dietary fiber, may represent a mechanism through which pre-biotics restore gut barrier function and attenuate the obesogenic effects of a HF diet.
- We sought to determine whether butyrate influences food intake, body weight, adiposity, and sensitivity to CCK in the face of a HFD.

Feeding behavior experiment timeline

<table>
<thead>
<tr>
<th>START 6-hr fast</th>
<th>Inject CCK/saline IP</th>
<th>Give food</th>
<th>Weigh food</th>
<th>Weigh food</th>
<th>Weigh food</th>
<th>END</th>
</tr>
</thead>
<tbody>
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Hypothesis & Methods

Hypothesis: Butyrate preserves CCK sensitivity in the vagal afferent pathway, reduces food intake, and attenuates increases in body weight and adiposity in rodent HFD-induced obesity.

Methods:
- Male C57BL/6j mice (5-6 wk old), in 2 cohorts of 24 mice each, received low-fat (LF) or high-fat (HF) diets for 6 weeks.
- Butyrate was provided as 0.25% monobutyrin (a stable analogue of butyrate) in drinking water to half of each diet group for 6 weeks.
- Food intake (per cage) and body weight were recorded weekly.
- Feeding behavior experiments were conducted in weeks 4 & 6 (Fig. 2).
- Mice were sacrificed for tissue collection at the end of the 6th week.

HFD-induced body weight gain and adiposity are unaffected by monobutyrin

Hypothetical blocks and arrows indicate the effects of butyrate on body weight gain and adiposity in the HFD-fed group compared to the control (LF) group.