

# Distal versus proximal intestinal short-chain fatty acid release in man

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propionate delivery to the human colon reduced energy intake and body weight gain.

In light of these important effects of SCFA, insight into their fate after bacterial production and/or intestinal absorption will help to improve the development of nutritional strategies aiming at modulation of intestinal SCFA. We addressed this issue by assessing SCFA release in the proximal intestines (jejunum, ileum and proximal colon) versus the distal intestines (descending colon, sigmoid and rectum) in man. Blood was simultaneously sampled from the portal vein, hepatic vein, superior mesenteric vein (SMV; draining the proximal intestines), inferior mesenteric vein (IMV; draining the distal intestines) and the radial artery in 20 patients undergoing upper abdominal surgery (see online supplementary table for patient characteristics).

SCFA concentrations were highest in the IMV and lowest in the radial artery (table 1). Acetate concentrations in the IMV and SMV were strongly correlated ( $r_s=0.57$ ,  $p<0.001$ ), but propionate and butyrate concentrations were not ( $r_s=-0.05$ ,  $p>0.05$ ;  $r_s=0.18$ ,  $p>0.05$ , respectively). Arterial acetate concentrations correlated with those in the IMV and the portal vein ( $r_s=0.65$ ,  $p<0.01$ ;  $r_s=0.58$ ,  $p<0.01$ , respectively) but not with those in the SMV ( $r_s=0.31$ ,  $p>0.05$ ). Neither propionate nor butyrate concentrations in the different veins and the radial artery were correlated. Importantly, propionate and butyrate release by the distal intestines were ~3-fold higher than observed for the proximal intestines (propionate:  $-63.8\pm 13.4$  vs  $-18.5\pm 3.5$   $\mu\text{mol/L}$ , butyrate:  $-62.1\pm 13.3$  vs  $-21.8\pm 7.4$   $\mu\text{mol/L}$ ), and acetate was only released to a significant extent by the distal intestines ( $-79.9\pm 25.5$   $\mu\text{mol/L}$ ). The liver showed a significant uptake of all SCFA (figure 1).

The higher SCFA release by the distal intestines relative to the proximal intestines may be explained in several ways. First, the mucosa of the proximal intestines may metabolise a relatively larger fraction of SCFA.<sup>5</sup> Second, differences in

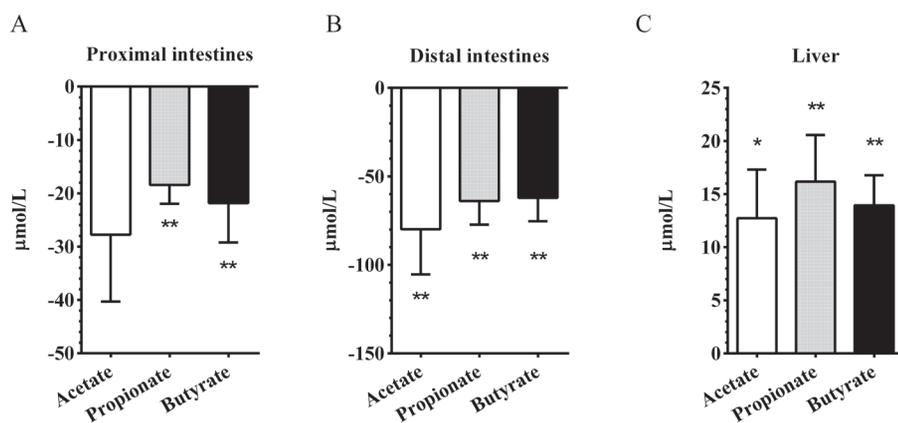
## Distal versus proximal intestinal short-chain fatty acid release in man

Several recent studies published in *Gut* highlight the potential of prebiotics and short-chain fatty acids (SCFAs) to improve obesity and its associated metabolic disorders. Catry and colleagues<sup>1</sup> demonstrated that inulin-type fructans improve endothelial dysfunction, and Roager *et al*<sup>2</sup> showed that a whole grain-rich diet reduced body weight and inflammation. Li *et al*<sup>3</sup> reported that butyrate administration reduced appetite and activated brown adipose tissue in mice, and Chambers and colleagues<sup>4</sup> showed that targeted

**Table 1** Arterial and venous SCFA concentrations

Concentrations ( $\mu\text{mol/L}$ )	Radial artery	Hepatic vein	Portal vein	Superior mesenteric vein	Inferior mesenteric vein
Acetate	21.8 $\pm$ 7.6	23.6 $\pm$ 4.8	41.4 $\pm$ 7.8	50.4 $\pm$ 11.3	102.7 $\pm$ 27.2
Propionate	1.0 $\pm$ 0.2	2.8 $\pm$ 0.8	24.5 $\pm$ 6.1	19.5 $\pm$ 3.5	64.8 $\pm$ 13.4
Butyrate	0.8 $\pm$ 0.2	2.6 $\pm$ 0.8	21.1 $\pm$ 4.4	22.7 $\pm$ 7.4	62.9 $\pm$ 13.4

SCFA, short-chain fatty acid.



**Figure 1** Arteriovenous differences in SCFA concentrations across (A) proximal intestines, (B) distal intestines and (C) liver. Positive values indicate net SCFA uptake, while negative values indicate net release. Asterisks indicate statistically significant uptake or release (\* $p < 0.05$ ; \*\* $p < 0.001$ ). SCFA, short-chain fatty acid.

local SCFA production may play a role. Indeed, the number of bacteria is highest in the colon, and gut microbiota composition and activity differ substantially between the proximal and distal intestines.<sup>6</sup> However, SCFA concentrations are higher in the proximal intestinal lumen.<sup>7</sup> Third, apical and basolateral epithelial cell uptake and transport of SCFA may differ between intestinal segments. To shed light on the importance of each of these potential mechanisms, studies combining analysis of the microbiota, intestinal/faecal SCFA concentrations, mucosal SCFA uptake and SCFA release are warranted.

These findings have implications for the development of nutritional strategies to modulate SCFA production and improve metabolic health: (1) slowly fermentable fibres that increase SCFA specifically in the distal intestines are expected to have higher potential for influencing host metabolism given the much higher SCFA release by the distal intestines, in line with the data of Chambers *et al*<sup>4</sup> and our recent work demonstrating that distal but not proximal acetate infusion promotes fat oxidation.<sup>8</sup> (2) Given the substantial SCFA uptake by the liver, metabolic processes such as lipogenesis, gluconeogenesis and oxidation can be influenced by modulation of intestinal and portal SCFA levels through non-digestible carbohydrates or specific bacteria, depending on nutritional status. (3) Assessing systemic acetate levels might represent a practical way to monitor the efficacy of acetogenic dietary fibres directed to influence overall host metabolism, since arterial acetate concentrations correlate with those in the IMV and the portal vein.

Evelien PJG Neis,<sup>1,2</sup> Hans MH van Eijk,<sup>1</sup> Kaatje Lenaerts,<sup>1</sup> Steven WM Olde Damink,<sup>1,3</sup> Ellen E Blaak,<sup>2,4</sup> Cornelis HC Dejong,<sup>1,2,3,5</sup> Sander S Rensen<sup>1</sup>

<sup>1</sup>Department of Surgery, NUTRIM School for Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, The Netherlands

<sup>2</sup>Top Institute Food and Nutrition, Wageningen, The Netherlands

<sup>3</sup>Department of Surgery, Universitätsklinikum Aachen, Aachen, Germany

<sup>4</sup>Department of Human Biology, NUTRIM School for Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, The Netherlands

<sup>5</sup>GROW School for Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands

**Correspondence to** Sander S Rensen, Department of Surgery, Maastricht University Medical Centre, PO Box 616, 6200 MD, Maastricht, The Netherlands; s.rensen@maastrichtuniversity.nl

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**Patient consent** Obtained

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Declaration of 1975 and in accordance with the Medical Research Involving Human Subjects Act (WMO). All patients provided verbal and written informed consent before surgery.

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