



Reply to Pattou et al. GASTRO-D-16-00421

Maude Le Gall, André Bado, Jean-Baptiste Cavin

► **To cite this version:**

Maude Le Gall, André Bado, Jean-Baptiste Cavin. Reply to Pattou et al. GASTRO-D-16-00421. Gastroenterology, WB Saunders, 2016, <10.1053/j.gastro.2016.05.043>. <inserm-01346607>

HAL Id: inserm-01346607

<http://www.hal.inserm.fr/inserm-01346607>

Submitted on 19 Jul 2016

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Reply to Pattou et al. GASTRO-D-16-00421

Maude LE GALL^{1*}, André BADO¹, Jean-Baptiste CAVIN¹

1 INSERM U1149, DHU Unity, Paris Diderot University, 75018, France

*Corresponding author:

Maude Le Gall Ph.D.

Gastrointestinal and Metabolic Dysfunctions in Nutritional Pathologies

Centre de Recherche sur l'Inflammation Paris Montmartre

Inserm UMRS 1149, Université Paris Diderot Paris 7,

Faculté de Médecine Site Bichat

16, rue Henri Huchard,

75890 Paris Cedex 18, France

Email:maude.le-gall@inserm.fr

Tel: +33 (0)157 277 459

Fax: +33 (0)157 277 471

Conflicts of interest:

The authors disclose no conflicts.

Words: 718

References: 7

We thank Pattou, Daoudi and Baud for their interest in our work¹, as well as for their complementary work², on intestinal absorption of ingested glucose after Roux-en-Y Gastric Bypass (RYGB). Based on their recent data obtained with a minipig model of RYGB, they claim this bariatric surgery to affect postprandial glucose metabolism primarily by modulating sodium-glucose intestinal cotransport. They further propose this hypothesis as an “alternative explanation” of our previous data obtained in a rat model and in human subjects who underwent RYGB surgery.

First of all, and contrary to what is stated in the above Letter, we never concluded in Cavin *et al.*¹ that “RYGB does not modify the uptake of ingested glucose”. Our *ex vivo* studies on intestinal transport revealed that greater amounts of ingested glucose remain within the Roux limb mucosa, as shown by increased luminal glucose uptake and increased SGLT-1 activity when compared to sham rats¹. *In vivo*, such a retention may result in a reduced transfer of ingested glucose to the blood.

While Baud *et al.* explored glucose transport in an elegant model of RYGB, a direct comparison with sham minipigs would have been even more informative. Such a comparison would allow distinguishing whether the observed variations of glucose transport are proper to RYGB surgery or just representative of the effect of bile and NaCl on physiological glucose absorption.

The major conclusion of Baud *et al.* is that the meal-derived glucose was absorbed only in the common intestinal limb where food meets bile and other gastrointestinal fluids. However, in their clamping experiment of RYGB minipigs, glycemia increases from 95 to 115 mg/dL (i.e., +20 mg/dL) when glucose is held in the Roux limb, while glycemia increases from 115 to 140 mg/dL (i.e., +25 mg/dL) when glucose reaches the common intestinal limb. This result clearly indicates that glucose is absorbed – and transferred to the blood – not only in the common intestinal limb but also in the Roux limb.

As far as the essential role of sodium in intestinal glucose transport claimed by Baud *et al.*, it is mainly based on two observations in their minipig model of RYGB. First, they did not detect any sodium in the Roux limb. The lack of data in the duodenum and jejunum of fasted (sham) minipigs impairs the interpretation of this experiment. More importantly, the microclimate adjacent to the intestinal brush border (aka, “the unstirred water layer”) is known to retain a high sodium concentration even when luminal sodium concentration is markedly reduced. Saltzman *et al.*³ did demonstrate *in vivo* that glucose absorption was minimally affected when the sodium concentration in the lumen was as low as 2.5 instead of 140 mEq/L. Second, Baud *et al.* showed that addition of NaCl (or bile) in isolated alimentary limb spontaneously increased glucose uptake. It would have been necessary to directly compare glucose uptake in the presence or absence of exogenous NaCl (or bile). In addition; “a significant part of the endogenous intestinal sodium originates in the stomach with bicarbonate secretion”, as mentioned by the authors themselves. The gastric pouch created by RYGB is still functional and gastric secretions are likely to be conserved after surgery⁴. Moreover, in everyday life, a non-negligible quantity of sodium is absorbed during meals (e.g., 3.6 g/day in the US)⁵. It is thus difficult to extrapolate the results obtained in isolated alimentary limb of fasted minipigs to what happens during meals in RYGB patients.

Finally Baud *et al.* reported that addition of 2 g of NaCl in a mixed meal of conscious RYGB minipigs doubles their postprandial glucose excursion. Once again a direct comparison with sham minipigs is lacking. Nevertheless this dramatic result suggests for the first time a considerable effect of exogenous NaCl in glucose absorption after RYGB since it is far greater than previously observed in non-operated minipigs⁶ or humans⁷.

In conclusion, we are really impressed by the work done by Baud *et al.* despite the lack of controls, which impairs the thorough analysis of their data. Even if the hypothesis proposed by Pattou, Daoudi and Baud to explain their data and ours is appealing, at the present stage we would be very careful in saying that the alimentary limb cannot absorb glucose. We would be even more careful in defining this feature as a determinant factor of postprandial glucose response in RYGB patients.

1. Cavin, J.-B. *et al.* Differences in Alimentary Glucose Absorption and Intestinal Disposal of Blood Glucose Following Roux-en-Y Gastric Bypass vs Sleeve Gastrectomy. *Gastroenterology* (2015). doi:10.1053/j.gastro.2015.10.009
2. Baud, G. *et al.* Bile Diversion in Roux-en-Y Gastric Bypass Modulates Sodium-Dependent Glucose Intestinal Uptake. *Cell Metab.* **23**, 547–553 (2016).
3. Saltzman, D. A., Rector, F. C. & Fordtran, J. S. The role of intraluminal sodium in glucose absorption in vivo. *J. Clin. Invest.* **51**, 876–885 (1972).
4. Arapis, K. *et al.* Remodeling of the Residual Gastric Mucosa after Roux-En-Y Gastric Bypass or Vertical Sleeve Gastrectomy in Diet-Induced Obese Rats. *PLoS ONE* **10**, e0121414 (2015).
5. Institute of Medicine (US) Committee on Strategies to Reduce Sodium Intake. *Strategies to Reduce Sodium Intake in the United States*. (National Academies Press (US), 2010).
6. Ehrlein, H., Haas-Deppe, B. & Weber, E. The Sodium Concentration of Enteral Diets Does Not Influence Absorption of Nutrients but Induces Intestinal Secretion of Water in Miniature Pigs. *J. Nutr.* **129**, 410–418 (1999).
7. Thorburn, A. W., Brand, J. C. & Truswell, A. S. Salt and the glycaemic response. *Br. Med. J. Clin. Res. Ed* **292**, 1697–1699 (1986).