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Early antibiotic-induced alteration of gut microbiota colonization affects gut adaptation in adult offspring

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Maternal environment during pregnancy and lactation influences health of the offspring and its microbiota[1]. Antibiotics use in pediatric practices is recognized to deeply affect gut barrier function and to disrupt the normal process of antigen presentation and handling[2]. However less is known on the long-term consequences of early alteration of gut colonization. Our aim was to investigate gut barrier function and GALT response to LPS in piglets born from sows whose microbiota had been manipulated by antibiotics. Long-term consequences on gut adaptation to a high-fat (HF) diet were examined in adult offspring. Sows were given amoxicillin per os (ATBQ, n=11 vs. CTRL, n=12) from 10 days before to 21 days after parturition. One piglet per litter was sacrificed at post-natal day (PND) 14, 21 and 28. The remaining piglets were given either a low fat (LF) or a HF diet from PND140 to 170. At PND14, increased ileal permeability in ATBQ piglets was associated with altered cholinergic regulation, and decreased mucosal acetylcholine concentration in ATBQ vs. CTRL. At PND21, TNFα secretion of LPMCs in response to LPS was observed in ATBQ piglets, but not in CRTL. HF diet did not affect glucose tolerance at PND170. However, while ileal permeability was increased in HF-fed CTRL pigs compared to LF-fed ones, no such increase was observed in ATBQ animals, and carbachol-induced permeability was only effective in LF-fed CTRL pigs. Secretion of TNFα by ileal explants stimulated by pokeweed mitogen was blunted in ATBQ pigs compared to CTRL ones, irrespective of the diet. Moreover, TNFα secretion by ileal explants was not increased in response to LPS in HF-fed ATBQ pigs as opposed to LF-fed ATBQ pigs or LF-and HF-fed CTRL pigs. Manipulating the maternal microbiota modified both ileal barrier function and GALT response to LPS during the neonatal period. It also deeply influenced the intestinal adaptive response to a HF diet in adult offspring, suggesting a microbiota imprinting in gut response to a HF diet.

Key-Words: Adaptative responses, Developmental origins of adult health, Large animals, Immune function, microbiota

1. F. Fåk et al. Am J Physiol., 294:G148-54, 2008.
2. A. Schumann et al. Physiol Genomics 23:235-45, 2005.

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