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PROCEEDINGS

Fatty acid composition as an early determinant of childhood obesity

Gérard Ailhaud · Florence Massiera · Jean-Marc Alessandri · Philippe Guesnet

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Recent evidence from animal and human studies favor the possibility that changes in the balance of essential PUFAs are altering the early stages of adipose tissue development, not only during fetal life and infancy which are periods showing the highest adaptability and vulnerability to external factors but also afterwards. Consistent with these data, cellularity of human adipose tissue from obese patients depends on the age of obesity onset, particularly the adipocyte number more than the adipocyte size, in agreement with the fact that only precursor cells divide and that adipose tissue expands dramatically at early age [2]. Both in rodents and humans, long-chain fatty acids act at the preadipocyte stage and trigger the formation of adipocytes. Fatty acids as well as eicosanoïds, i.e. prostaglandins and leukotrienes arising from arachidonic acid (ARA) metabolism, behave as activators/ligands of PPAR β/δ and PPARγ [3]. In vitro, ARA (arising in vivo from the metabolism of linoleic acid (LA) or from dietary and endogenous sources) plays an additional role as precursor of prostacyclin, and the adipogenic effect of prostacyclin takes place only at the preadipocyte stage [4, 6, 7]. Based upon these data, in vivo experiments have been performed to investigate whether a LA-enriched diet modulates fat mass. Under *isoenergetic* conditions, comparative experiments have been performed with wild-type (WT) mice and mice invalidated for the cell surface prostacyclin receptor (*ip–/–* mice). Both WT and *ip–/–* mice were fed during pregnancy and the suckling period high-fat diets either enriched with 15% (LA diet) or with 10% corn oil and 5% perilla oil containing α-linolenic acid (LNA) (LA/LNA diet). We have shown that (1) pups from WT mothers fed LA diet are 40% heavier 1 week after weaning than those from mothers fed LA/LNA diet or standard diet, (2) the LA-induced enhancement of fat mass is abolished in *ip–/–* mice, demonstrating the critical role of the prostacyclin receptor in excessive adipose tissue development, and (3) this effect of LA diet is confined to the gestation/lactation period. Importantly, the weight difference between mice fed LA and LA/LNA diet is maintained at the adult age [5]. In other words, PUFAs of the n-6 and n-3 series are *NOT* equipotent in promoting adipogenesis in vitro and adipose tissue development in vivo. Adipocytes once formed exhibit little or no turnover in the body and self-renewal and proliferation of adipocyte precursors are most likely events to occur. Therefore changes over decades in the fatty acid composition of dietary fats observed in breast milk and formula milk, i.e. a high increase in LA with slight or no change in LNA, may be responsible, at least in part, of the dramatic increase in the prevalence of childhood overweight and obesity [1]. Similar changes observed in most consumed food products can be traced to changes in human food habits but also in the feeding pattern of breeding stock. Whether prevention of obesity appears

G. Ailhaud (✉) · F. Massiera
Laboratoire Biologie du Dèveloppement du Tissu Adipeux,
Centre National de la Recherche Scientifique,
Faculté des Sciences, Université de Nice - Sophia Antipolis,
Parc Valrose, 28 Avenue de Valrose,
06108 Nice cédex 2, France
e-mail: Gerard.ailhaud@unice.fr

J.-M. Alessandri · P. Guesnet
INRA, CRJ, lab. nutrition sécurité alimentaire,
78352 Jouy-en-Josas, France

critical to avoid difficult if not insurmountable health problems to solve in the future, the status of lipids should therefore be reconsidered from the very beginning of the food chain.

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