

Biosynthesis of arachidonic acid (20:4n -6) in the liver of obese Zucker rats

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Jp Blond, Jm Cao, J Bezard. Biosynthesis of arachidonic acid (20:4n -6) in the liver of obese Zucker rats. Reproduction Nutrition Development, 1994, 34 (6), pp.634-635. hal-00899718

HAL Id: hal-00899718 https://hal.science/hal-00899718

Submitted on 11 May 2020

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	R+				R –			
-	Control mean	DFF mean	DFF + PPL mean	RSD	Control mean	DFF mean	DFF + PPL mean	. RSD
Food intake (g/day)	125 ^a	58°	54°	8.8	75b	47°	38°	5.9
Heat production ^a Respiratory quotient	409 ^a 0.94 ^a	399 ^a 0.82 ^b	361 ^b 0.80 ^b	9.7 0.01	286 ^c 0.93 ^a	303º 0.84b	294° 9 0.81 ^b	7.5 0.01
Diet -induced thermogenesis (% EMi) ^a	23.6ª	44.4 ^b	37.3 ^b	5.7	10.3°	23.2ª	24.8ª	8.9

Table I. (JF Gabbarou, PA Geraert)

^a Heat production (HP) in kJ/kg^{0.75}.d. Diet-induced thermogenesis = (fed HP – fasted HP) / metabolisable energy intake. Mean values with different letters were significantly different (p < 0.05). RSD: residual standard deviation.

β-adrenergic and serotoninergic control of diet-induced thermogenesis in birds. JF Gabarrou, PA Geraert (*INRA*, Station de Recherches Avicoles, 37380 Nouzilly, France)

Two experimental lines have been divergently selected for high (R+) or low (R-) residual feed intake [Bordas *et al* (1992) *Br Poult Sci* 33, 741-754]. Observed feed intake differed by 40% in males for the same bodyweight, and by 20% in females for the same bodyweight and the same egg-mass produced.

Energy balance measurements showed that basal metabolic rate did not differ between lines while diet-induced thermogenesis (DIT) or heat increment appeared significantly increased in R+ males compared to R- males: +84% if expressed as the difference between fed and fasted heat production [Geraert *et al* (1992) *Proc Nutr Soc* 51, 86A]. The energy balance of the females appeared similar, divergence in heat increment reached +133%.

Recent works in mammals suggest that part of the DIT is under sympathetic or β -adrenergic control. In the R+ and R- experimental lines, oral administration of DL-propranolol, a non-specific β -blocking agent (PPL, 5 mg/kg) reduced heat production in R+ birds but not in R-. Central control of DIT has also been investigated using Dfenfluramine, a 5-HT agonist (DFF, 10 mg/kg), well known for its thermogenic and thermolytic properties (table I). Combined stimulation of thermogenesis by fenfluramine and β -adrenergic blocking effect of propranolol (DFF+PPL) was also studied in females of both lines (table I).

The anorectic effect of DFF seems more important in the R+ line. Indeed, their feed intake was reduced to the level of the R- genotype. While the thermogenic effect of DFF did not differ between lines, propranolol significantly reduced heat production only in R+ hens (-9.5%) without any effect in the R-birds. The divergence in dietinduced thermogenesis between genotypes is partly under sympathetic control, while serotonin (5-HT) is more involved in the regulation of feed intake than thermogenic abilities.

V. Genetic-nutrition interactions

Biosynthesis of arachidonic acid (20:4n –6) in the liver of obese Zucker rats. JP Blond, JM Cao, J Bezard (*Nutrition Cellulaire et Métabolique, Université de Bourgogne, BP 138, 21004 Dijon Cedex, France*)

The genetically obese Zucker rat is characterized by a lower level of arachidonic acid (20:4n – 6), in hepatic lipids (expressed as a percentage of total fatty acids), than in the lean animal, in agreement with a partial inhibition of $\Delta 6$ and mainly $\Delta 5$ microsomal desaturation [Blond *et al* (1989) *Lipids* 24, 389-395; Guesnet *et al* (1990) *Lipids* 25, 517-522]. The aim of this study was to investigate whether treatment with a hypocholesterolemic drug (simvastatin, which stimulates fatty-acid metabolism) or the addition of borage oil (which contains γ -linolenic acid (18:3n–6), the $\Delta 6$ desaturation product) in the diet can facilitate the biosynthesis of 20:4n–6 from linoleic acid (18:2n–6), *in vitro* and *ex vivo*.

In a first set of experiments, male rats of the Zucker strain were divided into 4 groups of 6 animals: 2 groups of untreated, obese and lean, and 2 groups of treated animals. They received a daily dose of 2 mg/kg body weight of simvastatin in 0.1 ml of corn oil by gastric intubation for 13 d. All the animals were killed on day 14. In the second set of experiments, rats were also divided into 4 groups of 6 animals each, 2 groups were maintained for 12 weeks on a diet (5% w/w fat) containing borage oil (18:2 + 18:3n–6), whereas the other groups continued to receive the control diet (5% w/w fat) with 18:2n–6 only. The food intake was adjusted to 20 g/d/rat.

The animals were killed and the liver microsomes were isolated. The conditions of desaturase assay and fatty-acid analysis (GLC and HPLC) were essentially those previously described [Maniongui *et al* (1993) *Lipids* 28, 291-297]. Saturating levels of ¹⁴C substrates were used (120 nmol of ¹⁴C 18:2n–6 and 80 nmol of ¹⁴C 20:3n–6).

Treatment with simvastatin did not change ∆6 desaturase specific activity (SA) in either phenotype, but increased ∆5 desaturase SA in obese rat (+28%). The same effect had been observed with fenofibrate, another hypolipidemic drug [Blond et al (1989) Biochem Pharmacol 38, 2741-2744]. However, 18:3n-6 supplementation increased (+39.7%) Δ6 desaturase SA in the liver of the obese rats only. The changes in the rates measured in vitro were not accompanied by an increase in the level of 20:4n-6 in liver microsomal phospholipids. Our results suggest that the experimental conditions (2 mg simvastatin for 13 d or 45 mg/d/rat 18:3n-6 for 12 weeks) were beneficial by increasing both desaturase activities in vitro but were unable to restore a fatty-acid profile in obese rats close to that observed in lean rats. Because of the relatively low turnover of phospholipids, prolonged treatment with simvastatin or 18:3n-6 supplementation may be beneficial by increasing the production of n-6 polyunsaturated fatty acids in vivo.

Growth of muscle satellite cells isolated from chickens of 2 lines divergently

selected for fast or slow growth. MJ Duclos, B Chevalier, FH Ricard, J Simon (INRA-Tours, Station de Recherches Avicoles, 37380 Nouzilly, France)

Fast and slow growing lines of chickens (FG and SG) have been divergently selected [Ricard (1975) *Ann Genet Select Anim* 7, 427-443]. At hatching, chicks of both lines weight about the same but as growth proceeds, FG chickens are always heavier than SG at the same age. They also have significantly heavier muscles associated with larger muscle fibers [Rémignon *et al* (1994) *Br Poult Sci* 35, 65-76]. The fact that muscle fiber growth is paralleled by an increase in the number of nuclei, due to the fusion of multiplying muscle satellite cells with existing fibers, suggests that satellite cells from those selected lines may have different growth potential.

Satellite cells were preparated from pectoralis muscles of day-old male chicks and DNA synthesis was measured by ³H-thymidine (³H-THY) incorporation as described in Duclos et al [(1991) J Endocrinol 128, 35-42]. The metabolism of satellite cell derived myotubes was studied. 3Haminoisobutyric acid (3H-AIB) or 3H-deoxy-D-glucose (³H-DG) uptake was measured following 4 h preincubation in DMEM 0.5% bovine serum albumin (DMEM/BSA) in the presence or absence of IGF-1. Protein synthesis was measured by ³Htyrosine (3H-TYR) incorporation into proteins under similar conditions. For protein degradation studies. myotubes were incubated for 3 d in the presence of ³H-TYR to label proteins, and after washing, the release of ³H-TYR was subsequently monitored over 24 h. Data from 4-8 independent experiments, with a minimum of triplicate determinations per treatment within each experiment, were analysed by ANOVA and are presented as mean ± standard error of the mean.

DNA synthesis was stimulated by fetal calf serum (FCS, 0.3 – 10%) in a dose-dependent manner in satellite cells from both lines. The maximal stimulation was significantly higher ($F_{(1.240)} = 197$, P < 0.01) in cells from FG chicks ($432 \pm 39\%$ of basal with 2.5% FCS) than in cells from SG chicks ($317 \pm 22\%$). DNA synthesis was also stimulated by IGF-1 (10 or 100 ng/ml) and a significantly larger stimulation was observed in FG than SG cells ($F_{(1.72)} = 20.5$, P < 0.01; 263 $\pm 20\%$ of basal compared to 213 $\pm 22\%$ with 100 ng IGF-1/ml, respectively).

None of the metabolic parameters differed between lines under basal conditions