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Neonatal leptin exposure induces altered expression of specific PPARα transcripts in adipose tissue of adult rats

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Administration of leptin to neonatal offspring of rats exposed to 70% global undernutrition (UN group) during pregnancy prevents increased weight gain when fed a high-fat diet after weaning compared with the offspring of pregnant dams fed *ad libitum* (AL group)[(1)]. Administration of leptin to adult rats induces a transient increase in PPARα mRNA expression and up-regulation of fatty acid β-oxidation in adipose tissue, and weight loss[(2)]. The present study has tested the hypothesis that neonatal leptin exposure persistently alters the expression of PPARα in adipose tissue.

Female offspring born to AL or UN dams received 2.5 μg leptin/g weight per d or saline (9 g NaCl/l) between 3 and 13 d after birth. Offspring were weaned onto a high-fat diet (45% energy; lard–soybean oil 7:1, w/w) and abdominal adipose tissue was collected on postnatal day 170[(1)]. 5′ RNA ligase-mediated rapid amplification of cDNA ends identified three alternative PPARα mRNA transcripts and 5′ regulatory regions within the *PPARα* gene were identified; i.e. promoters (P)1, P2 and P3. Cloning of these promoters into a luciferase reporter vector system showed that activity of P2, but not P1 and P3, was induced in a dose-dependent manner by leptin and the PPARα agonist clofibric acid. mRNA expression of the individual PPARα transcripts and of the fatty acid β-oxidation target genes carnitine palmitoyl transferase (CPT)-1 and acyl-CoA oxidase (AOX) were measured by real-time RT–PCR. PPARα P2 expression was higher in adipose tissue of rats exposed neonatally to leptin irrespective of maternal diet during pregnancy, while P1 was expressed at the same level independent of neonatal leptin treatment. P3 expression was barely detectable in adipose tissue.

		mRNA expression in adipose tissue (relative to AL (%))								
		AL				UN				
		Saline (*n* 8)		Leptin (*n* 8)		Saline (*n* 8)		Leptin (*n* 8)		ANOVA:
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	*P*<
PPARα:	P2	100	9.5	232***	10.2	74.3	15.8	218***	26.7	0.0001
	P1	100	8.5	98.6	8.3	103	13.0	95.4	8.6	NS
CPT-1		100	12.0	350***	28.0	99.8	5.1	302***	61.0	0.0001
AOX		100	11.2	729***	106	105	15.0	565***	94.0	0.0001

Mean values were significantly different from those for the AL saline group (one-way ANOVA with Dunnett's *post hoc* correction): ***$P<0.0001$.

These data show that, unlike adults, neonatal exposure to leptin induces persistent up-regulation of PPARα expression, and of its targets CPT-1 and AOX. The leptin effect was specific to the PPARα P2 promoter, which implies a leptin-induced shift in PPARα promoter use in adipose tissue. Together these results suggest that leptin exposure in early life may be an important determinant of fatty acid metabolism in adipose tissue.

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