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Do very small adipocytes in subcutaneous adipose tissue (a proposed risk factor for insulin insensitivity) have a fetal origin?

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SUMMARY

Background & aims: Previous studies have shown that fetal life malnutrition affects preferences for fat deposition in the body thereby predisposing for visceral adipocity and associated disorders in glucose-insulin regulation. In this study, we aimed to test the hypotheses that late-gestation undernutrition 1) has long-term differential impacts on development, expandability and metabolic features in subcutaneous as compared to perirenal and mesenteric adipose tissues, which 2) will predispose for visceral obesity upon exposure to an obesogenic diet in early postnatal life.
Methods: Twin-bearing last trimester ewes received diets supplying 100% (NORM) or 50% (LOW) of protein and energy requirements. Lambs received moderate, low-fat (CONV) or high-carbohydrate-high-fat (HCHF) diets from 3-days until 6-months of age (just after puberty), and then half the lambs (including all males) were sacrificed. Remaining animals (exclusively females) received a low-fat, grass-based diet until sacrificed at 2-years of age (adulthood). In subcutaneous, perirenal and mesenteric fat, energy metabolism related gene expressions and fatty acid composition were

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determined. Histological evaluations were performed of subcutaneous and perirenal fat. The late-gestation undernutrition reduced whole-body insulin sensitivity and increased the risk of obesity-induced mesenteric adiposity in the sheep used in the experiment.
Results: A deviating morphology of subcutaneous adipose tissue with greater occurrence of very small adipocytes (<40 μm in diameter) and collagen infiltration was observed in the non-obese LOW/CONV lambs, and after dietary correction (and associated body fat loss) it became apparent in all adult LOW sheep. LOW lambs deposited more fat in visceral compared to subcutaneous fat when exposed to the obesogenic HCHF diet. Prenatal undernutrition had differential impacts in subcutaneous versus perirenal fat on expressions of glucose-insulin signaling and lipid metabolism genes and on fatty acid composition, but these prenatal impacts were not sustained into adulthood, except to a limited extent in perirenal fat, where C14:0 was decreased in LOW sheep.
Conclusions: The present study showed that greater preponderance of very small adipocytes, increased collagen infiltration and reduced subcutaneous lipid accumulation ability, as well as altered perirenal fat preferences for accumulation of C14:0 can have a fetal origin. Disturbance of normal (subcutaneous) adipose tissue development may play a key role in linking fetal malnutrition to disease risk later in life.

Abbreviations

ACTB	beta-actin
AMPK	AMP-activated kinase
CONV	moderate diet fed to lambs from 3 days to 6 months of age
FA	fatty acid
FAS	fatty acid synthase
FTO	fat mass and obesity associated protein
GLUT1 and GLUT4	glucose transporter 1 and 4
HCHF	high-carbohydrate-high-fat diet fed to lambs from 3 days to 6 months of age
INSRβ	insulin receptor beta subunit
IRS1	insulin receptor substrate 1
JNK	C-Jun N-terminal kinase
JSP1	JNK stimulatory phosphatase 1
LOW	50% maternal nutrition through late gestation
MESAT	mesenteric adipose tissue
MUFA	monounsaturated fatty acid
n-3 and n-6 PUFA	omega-3 and omega-6 polyunsaturated fatty acids
NORM	100% maternal nutrition through late gestation
PCA	principal component analyses
PFA	Paraformaldehyde
PPARα and PPARγ	peroxisome proliferator-activated receptor alpha and gamma
PRAT	perirenal adipose tissue
PUFA	polyunsaturated fatty acids
SUBAT	subcutaneous adipose tissue
UCP2	uncoupling protein 2
VEGF	vascular endothelial growth factor