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Gita L. Rahardjo
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Feeding, metabolic rate, and peptide YY regulation
in obese-prone and obese-resistant mice

Gita L. Rahardjo

B. Med. Sci.

A thesis submitted in fulfilment of the requirements
for the award of the degree

Master of Science (Research)

from

University of Wollongong



Faculty of Health & Behavioural Sciences

April 2009

Certification

I, Gita L. Rahardjo, declare that this thesis, submitted in fulfilment of the requirements for the award Master of Science (Research), in the Faculty of Health & Behavioural Sciences, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged.

The document has not been submitted for qualifications at any other academic institute.

Gita L. Rahardjo

April 2009

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Publications/Presentations

Publications

Rahardjo GL, Huang X-F, Tan YY, Deng C. 2007. Decreased plasma PYY accompanied by elevated PYY and Y2 receptor binding densities in the medulla oblongata of diet-induced obese mice. *Endocrinology* 148:4704-4710.

Huang XF, Liu Y, Rahardjo GL, McLennan PL, Tapsell LC, Buttemer WA. 2008. Effects of diets high in whey, soy, red meat and milk protein on body weight maintenance in diet-induced obesity in mice. *Nutr Dietetics* 65 (Suppl. 3):S53-S59.

Presentations

Rahardjo GL, Huang XF, Tan YY, Deng C. The role of PYY and H1 histamine receptor expression in chronic diet-induced obese and diet-resistant mice. Poster presented at: 7th IBRO World Congress of Neuroscience, 2007; Sydney.

Rahardjo G, Huang X, McLennan PL, Buttemer WA. Does obese-prone or resistant mouse differ in their feeding, metabolic rate, and peptide YY regulation? Poster presented at: 10th International Congress on Obesity, 2007; Sydney.

Rahardjo GL, Tan YY, Huang XF. NPY Y2 receptor binding density is reduced in the nucleus accumbens of mice resistant to diet-induced obesity. Oral presentation at: The 26th Annual Meeting of the Australian Neuroscience Society Incorporated, 2006; Sydney.

Rahardjo G, Buttemer W, Huang XF. Progressive change on oxygen consumption and energy intake during development of diet-induced obesity in mice. Oral presentation at: 14th Annual Scientific Meeting of Australasian Society for the Study of Obesity, 2005; Glenelg, South Australia.

Abbreviations

AGRP	Agouti-related peptide
ANOVA	Analysis of variance
Arc	Arcuate nucleus
ATP	Adenosine triphosphate
CART	Cocaine and amphetamine-regulated transcript
DIO	Diet-induced obese
DMH	Dorsomedial hypothalamus
DR	Diet-resistant
g	Grams
h	Hour
kJ	Kilojoule
L	Litre
LF	Low-fat
LH	Lateral hypothalamus
mL	Millilitre
mm	Millimetre
ng	Nanogram
nM	Nanomolar
NPY	Neuropeptide Y
pmol	Picomolar
POMC	Proopiomelanocortin
PYY	Peptide YY

RIA	Radioimmunoassay
RQ	Respiratory quotient
SD	Standard deviation
SEM	Standard error means
μ M	Micromolar
VMH	Ventrolateral hypothalamus

Abstract

Some individuals become obese while others remain lean on a high energy diet. The cause of this susceptibility to the development of diet-induced obesity is still unknown. Variations in energy intake, expenditure and the type of substrate being oxidised, as well as Peptide YY (PYY) system regulation are believed to contribute to differential susceptibility to the development of diet-induced obesity.

This project aimed to compare energy balance regulation including energy intake and expenditure, and the PYY system in diet-induced obese (DIO) and diet-resistant (DR) mice.

To investigate energy balance this project measured food intake, body mass gain, spontaneous activity, 24h-metabolic rates and body composition in DIO, DR and low-fat-fed (LF) mice. Plasma PYY was measured by radioimmunoassay and its central binding sites (Neuropeptide Y-Y1, 2 & 5 receptors) were measured by quantitative autoradiography.

This study has shown that body weight gain was significantly (50%) higher in DIO mice compared to DR and LF mice ($F_{2,32}=101.5$, $p<0.001$). The higher net energy gain in DIO mice was due to their significantly higher food intake compared to DR mice ($F_{2,33}=7.79$, $p=0.002$). There were no differences in the metabolic rate, spontaneous activity or type of substrate being oxidized between the DIO and DR mice. The levels of plasma PYY were 32% lower in the DIO mice than in LF mice ($p=0.007$). PYY and NPY-Y2 receptor binding densities in the DIO mice were significantly higher than DR mice (52% and 24%, respectively) and LF mice (44% and 37%, respectively) at the caudal medulla.

Overall, the major contributing factor to diet-induced obesity in this animal model was increased

energy intake, not a difference in energy expenditure, assimilation efficiency or the substrate types that were oxidized. Reduced plasma PYY in DIO mice may have resulted in the compensatory upregulation of PYY and NPY-Y2 receptor binding density in the caudal medulla. This may contribute at least partially towards the development of diet-induced obesity as this pathway suppresses food intake.

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