

Nutritional programming of behaviour in the rat

Contents

1.0 Introduction	1-63
<i>1.1.1 Obesity – definitions, diagnosis, prevalence, future projections, co-morbidities, causes and treatment</i>	1-9
<i>1.1.2 Definitions and diagnosis of obesity</i>	1-2
<i>1.1.3 UK prevalence of obesity and associated illness</i>	2-4
<i>1.1.4 Projected increases in the UK prevalence of obesity</i>	4
<i>1.1.5 Global trends in obesity</i>	4-5
<i>1.1.6 Clinical obesity and associated co-morbidities</i>	5-7
<i>1.1.7 Genes vs. environment</i>	7-8
<i>1.1.8 Treatment of obesity</i>	8-9
<i>1.2 Obesity and Behaviour</i>	9-23
<i>1.2.1 Diet, obesity and behaviour in humans</i>	9-15
<i>1.2.2 Diet, obesity and behaviour in rats</i>	15-16
<i>1.2.2.1 Emotional behaviour</i>	16-18
<i>1.2.2.2 Ingestive behaviour</i>	18-19
<i>1.2.2.3 Learning and memory</i>	19-23
<i>1.3. Fetal programming and the developmental origins of adult disease</i>	23-39
<i>1.3.1 Introduction</i>	23-26
<i>1.3.2 Epidemiological evidence for programming</i>	26-29

<i>1.3.3 Prevalence of obesity in women of child bearing age in the UK</i>	29-30
<i>1.3.4 Maternal dietary perturbations and programming in rodents</i>	30-36
<i>1.3.5 Possible mechanisms underlying programming</i>	36-39
1.4. Programming brain neurochemistry in rodents	39-45
1.5. Programming induced by changes to maternal behaviour	45-47
1.6 Nutritional programming of behaviour in the rat	47-59
<i>1.6.1 Anxiety and Exploratory behaviour</i>	48-49
<i>1.6.2 Learning and memory</i>	49-51
<i>1.6.3 Ingestive behaviour</i>	51-54
<i>1.6.4 Conclusion</i>	54
1.7 Aims and Hypothesis	60-63
Chapter 2 - The effect of maternal cafeteria diet feeding during critical periods of development upon metabolism and behaviour	64-108
2.0 Introduction	64-65
2.1 Experimental procedures	66-74
<i>2.1.1 Animal procedures</i>	66-68
<i>2.1.2 Weekly bodyweight and adipose tissue mass</i>	68-69
<i>2.1.3 Offspring carcass composition</i>	69

2.1.4 Plasma leptin serum concentration	70
2.1.4.1 Leptin ELISA	70-71
2.1.5 Analysis of behaviour	71
2.1.5.1 Elevated plus maze	71-73
2.1.5.2 Open Field	73-74
2.1.6 Statistical analysis	74
2.2 Results	75-95
2.2.1 Offspring bodyweight and adipose tissue mass	75-77
2.2.2 Offspring carcass composition	78-79
2.2.2.1 Males	78
2.2.2.2 Females	78
2.2.3 Plasma leptin	79-80
2.2.4 Elevated plus maze	80-88
2.2.4.1 Males	80-84
2.2.4.2 Females	85-88
2.2.5 Open Field	89-95
2.2.5.1 Males	89-91

2.2.5.2 Females	92-95
2.3 Discussion	96-108
Chapter 3 - The impact of maternal cafeteria diet feeding during lactation upon behaviour, brain turnover of 5-HT and DA in adult offspring	109-175
3.0 Introduction	109-113
3.1 Experimental Procedures	114-122
3.1.1 Animal procedures	114
3.1.2 Maternal macronutrient intake	115
3.1.3 Ingestive behaviour	115-117
3.1.3.1 Behavioural satiety sequence (BSS)	115-116
3.1.3.2 Micro-structural analysis and the BSS	116-117
3.1.4 Learning and memory	117-120
3.1.4.1 Open field habituation	117-118

<i>3.1.4.2 Novel object discrimination (NOD)</i>	<i>118-120</i>
<i>3.1.5 5-HT and DA concentrations and turnover</i>	<i>120-121</i>
<i>3.1.5.1 Brain neurotransmitter content and metabolism</i>	<i>120</i>
<i>3.1.5.2 High-performance liquid chromatography with electrochemical detection</i>	<i>121</i>
<i>3.1.6 Statistical analysis</i>	<i>121-122</i>
3.2 Results	<i>123-152</i>
<i>3.2.1 Maternal bodyweight and macronutrient intake</i>	<i>123-128</i>
<i>3.2.2 Offspring body weight</i>	<i>128-129</i>
<i>3.2.3 Behavioural satiety sequence</i>	<i>129-143</i>
<i>3.2.3.1 Test food intake and 1 hour behavioural scores</i>	<i>129-130</i>
<i>3.2.3.2 Behavioural measures of eating, grooming and resting (males)</i>	<i>130-132</i>
<i>3.2.3.3 Behavioural measures of eating, grooming and resting (females)</i>	<i>133-135</i>
<i>3.2.3.4 Microstructural analysis and BSS</i>	<i>136-138</i>

<i>3.2.3.5 Behavioural measures of rearing, locomotor and olfactory behaviour (Males)</i>	139
<i>3.2.3.6 Behavioural measures of rearing, locomotor and olfactory behaviour (Females)</i>	139
<i>3.2.3.7 Rearing, locomotor and olfactory behaviour microstructure (Males)</i>	140-141
<i>3.2.3.8 Rearing, locomotor and olfactory behaviour microstructure (Females)</i>	141
3.2.4 Open Field Habituation	144-145
<i>3.2.4.1 Males</i>	144
<i>3.2.4.2 Females</i>	144
3.2.5 Novel Object Discrimination	145-148
<i>3.2.5.1 Males</i>	145-146
<i>3.2.5.2 Females</i>	147-148
3.2.6 Brain neurotransmitter determination	148-152

3.3.0 Discussion	153-175
<i>3.3.1 Maternal macronutrient intake</i>	<i>153-154</i>
<i>3.3.2 Ingestive behaviour</i>	<i>154-159</i>
<i>3.3.3 Learning and memory</i>	<i>160-167</i>
<i>3.3.4 Brain neurotransmitters determination</i>	<i>167-169</i>
<i>3.3.5 Brain neurotransmitter determination and ingestive behaviour</i>	<i>169-172</i>
<i>3.3.7 Brain neurotransmitter determination and learning and memory</i>	<i>172-174</i>
<i>3.3.8 Conclusion</i>	<i>174-175</i>
4.0 Chapter 4 - General discussion	176-199
4.1 Introduction	176-177
4.2 Maternal overnutrition and offspring adiposity	177-179
4.3 Maternal overnutrition and behaviour	179-182
4.4 Why the lactation period?	182-186

<i>4.4.1 Maternal milk</i>	<i>182-184</i>
<i>4.4.2 Maternal behaviour</i>	<i>185-186</i>
<i>4.5 Brain neurochemistry data – meaning and limitations</i>	<i>187-189</i>
<i>4.6 Possibilities for future research</i>	<i>190-193</i>
<i>4.7 Notes on age</i>	<i>193</i>
<i>4.8 Strain comparisons</i>	<i>193-194</i>
<i>4.9 From rats to humans</i>	<i>194-198</i>
<i>4.10 Conclusion</i>	<i>198-199</i>
<i>References</i>	<i>200-248</i>

Figures	
Fig.2.1. Control chow vs. cafeteria diet.	67
Fig. 2.2. Schematic presentation of experimental design.	68
Fig. 2.3. Adipose tissue mass.	69
Fig. 2.4. The effect CD feeding upon post-weaning bodyweight in male and female offspring.	76
Fig. 2.5. The effect of pre-gestational (PG), gestational (G) and lactational (L) CD upon carcass composition in male and female offspring (fat content shown as wet weight).	79
Fig. 2.6. The effect of lactational CD upon plasma circulation of leptin in adult offspring.	80
Fig. 2.7. The effect CD feeding upon behaviour on the elevated plus maze in male offspring.	83
Fig. 2.8. The effect of CD feeding upon behaviour on the elevated plus maze in male offspring.	84
Fig. 2.9. The effect of CD feeding upon behaviour on the elevated plus maze in female offspring.	87
Fig. 2.10. The effect of CD upon behaviour on the elevated plus maze in female offspring.	88
Fig. 2.11. The effect of CD upon behaviour on the open field in male offspring.	91
Fig. 2.12 The effect of CD upon behaviour on the open field in male offspring.	92
Fig. 2.13. The effect of CD upon behaviour on the open field in female offspring.	94
Fig. 2.14. The effect of CD upon behaviour on the open field in female offspring.	95
Fig. 3.1. Schematic representation of the experimental design.	114
Fig. 3.2. A conventional behavioural satiety sequence (BSS) across a 1-hour observation period from our laboratory.	117
Fig. 3.3 Bodyweight of dams during the three week lactation period and macronutrient intake in mothers either fed cafeteria diet (CD) or control chow (C) during the first 10 days post-partum.	125

Fig. 3.4 Macronutrient intake in mothers either fed cafeteria diet (CD) or control chow (C) during the first 10 days post-partum and the amount of human food vs. chow diet consumed by CD mothers.	126
Fig. 3.5 Energy intake in mothers either fed cafeteria diet (CD) or control chow (C) during the first 10 days post-partum.	126
Fig. 3.6 Macronutrient intake in mothers either fed cafeteria diet (CD) or control chow (C) during the first 10 days post-partum.	128
Fig. 3.7 The effect of lactational cafeteria diet (CD) upon post weaning bodyweight development.	129
Fig. 3.8 The effect of lactational CD (black columns) upon intake of test mash.	130
Fig. 3.9 The effect of lactational CD upon eating parameters in males.	131
Fig. 3.10. The effect of lactational CD upon resting latency (A) resting duration (B) and grooming duration (C) in males.	132
Fig. 3.11 The effect of lactational CD upon eating parameters in females.	134
Fig. 3.12 The effect of lactational CD upon resting latency (A) resting duration (B) and grooming duration (C) in females.	135
Fig. 3.13 The effect of lactational CD upon the frequency of eating behaviour in males (A) and females (B) across the 1-hr test session.	137
Fig. 3.14 The effect of lactational CD upon duration of eating (thick line), resting (thin line) and grooming behaviours (dotted line) in males.	138
Fig. 3.15 The effect of exposure to CD throughout lactation upon duration of eating (thick line), resting (thin line) and grooming behaviours (dotted line) in females.	138
Fig. 3.16 The effect of lactational CD upon rearing, locomotor and olfactory behaviour in adult offspring.	140
Fig. 3.17 The effect of lactational CD upon rearing, locomotor and olfactory behaviour in adult male offspring across the 1-hour test session.	142
Fig. 3.18 The effect of maternal CD upon rearing, locomotor and olfactory behaviour in adult female offspring across the 1-hour test session.	143
Fig. 3.19 The effect of lactational CD upon habituation upon behaviour	145

the open field.	
Fig.3.20. The effect of lactational CD upon novel object discrimination in males.	146
Fig. 3.21 The effect of lactational CD upon novel object discrimination in females.	148
Tables	
Table 1.1 – Studies demonstrating the effects of direct and maternal dietary perturbations upon offspring behaviour in rats.	55-59
Table 2.1. Effect of pre-gestational (PG), gestational (G) and lactational (L) cafeteria diet on body weight and fat pads in female (F) and male (M) offspring as measured at 5 months of age.	77
Table 3.1 The effect of exposure to cafeteria diet throughout lactation upon dopamine (DA) and serotonin (5-HT) content and turnover in the hypothalamus.	150
Table 3.2 The effect of exposure to cafeteria diet throughout lactation upon dopamine (DA) and serotonin (5-HT) content and turnover in the hippocampus.	151
Table 3.4 The effect of exposure to cafeteria diet throughout lactation upon dopamine (DA) and serotonin (5-HT) content and turnover in the frontal cortex.	152
Abbreviations	
5-HT = 5-hydroxytryptamine (5-HT)	
5-HIAA = 5-Hydroxyindoleacetic acid	
α -MSH = alpha-Melanocyte-stimulating hormone	
ABN = Arched back nursing	
AgRP = Agouti-related peptide	

ARC = Arcuate nucleus	
BNST = Bed nucleus of the stria terminalis	
BSS = Behavioural satiety sequence	
CD = Cafeteria diet	
CART = Cocaine and amphetamine regulated transcript	
CRF = Corticotropin-releasing factor	
DA = Dopamine	
DMH Dorsomedial hypothalamus	
DOPAC = 3,4-Dihydroxyphenylacetic acid	
EPM = Elevated plus maze	
LC = Locus coeruleus	
LHA = Lateral hypothalamic area	
LG = Licking/ grooming	
MCH = Melanin concentrating hormone	
NAc = Nucleus accumbens	
NA = Noradrenaline	
NOD = Novel object discrimination	

NPY = Neuropeptide-Y	
OF = Open field	
OFH = Open field habituation	
POMC = Pro-opiomelanocortin	
PVN = paraventricular nucleus	
VTA = Ventral tegmental area	
VIDA = Variable interval delayed alteration	
VMH = Ventromedial hypothalamus	