Peripheral Hormone Concentrations and Food Intake Regulation in Obese (fa/fa) (Ob) and Lean (Le) Zucker Rats under Different Feeding Regiments

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Food intake is regulated by hunger, satiety and reward signals through various chemical messengers such as orexigenic and anorexigenic peptides/hormones, as well as brain neurotransmitters (Erlanson-Albertsson, 2005). These chemical messengers are found throughout the body in peripheral organs as well as in the brain (Erlanson-Albertsson, 2005). In the present study we characterized differences in plasma concentrations of the peptides insulin, leptin, amylin, peptide YY (PYY3-36), glucagon-like peptide 1 (GLP-1), cholecystokinin (CCK), cocaine and amphetamine-regulated transcript (CART) and ghrelin in Ob and Le Zucker rats exposed to different feeding regiments. Ob Zucker rats have a leptin receptor mutation that predisposes them to becoming obese and express diabetes, hyperphagia and hyperinsulinemia (Hamdi, 1992). We used male 1 month old rats, divided into the following 8 groups (n=3/group): 1) Ob U & Le U (fed an unrestricted amount of food), Ob R & Le R (fed 70% of the U rat diet) 2) Ob PU & Le PU (rats previously U (1 to 6 months) and then R (6 to 7 months), Ob PR & Le PR (rats previously R (1 to 6 months) and then U (6 to 7 months). At 7 months of age, 500 µl of blood were sampled from each animal under light isoflurane anesthesia 4 hrs into the dark cycle under two conditions: i)after a 24 hr fast & ii)3 hrs after feeding (animals were fasted 24 hrs prior to being exposed to 1 hr of unrestricted food access). Plasma was analyzed using enzyme immunoassay (EIA) kits and blood glucose, weight and food intake were also measured (Table 1). Our data indicate that circulating levels of the above peripheral messengers are influenced by feeding status as well as conditions such as hyperleptinemia, hyperinsulinemia, and body weight. Zucker rats have a unique dopamine D2 receptor profile (Michaelides et al, 2005) and therefore interactions between peripheral mechanisms and brain reward pathways may prove significant in future approaches towards treating obesity.

Table 1	***Ob U***		***Ob R***		***Le U***		***Le R***		***Ob PU***		***Ob PR***		***Le PU***		***Le PR***	
Average & (±SEM)	*Fast*	*Fed*	*Fast*	*Fed*	*Fast*	*Fed*	*Fast*	*Fed*	*Fast*	*Fed*	*Fast*	*Fed*	*Fast*	*Fed*	*Fast*	*Fed*
Weight *(g)*	712 (14.2)	718 (16.17)	511 (6.52)	519 (5.7)	438 (6.63)	447 (7.7)	331 (4.54)	336 (8.34)	623 (8.15)	631 (9.17)	692 (11.2)	701 (10.56)	356 (2.72)	365 (3.51)	424 (5.4)	431 (8.89)
Food Intake *(g)*		4.3 (0.27)		5.3 (0.75)		4.35 (0.55)		6.5 (1.16)		9.12 (0.8)		7.2 (0.77)		9.2 (0.8)		5.0 (0.45)
Blood Glucose *(mg/dL)*	115.7 (7.0)	146 (16.1)	112.3 (4.38)	134 (8.8)	78.5 (2.51)	88.5 (8.39)	66.4 (2.27)	94 (3.8)	103 (2.87)	139.5 (11.1)	111.7 (10.4)	130 (16.2)	62.5 (2.59)	90.25 (8.64)	79.5 (5.08)	107.7 (9.8)
Insulin *(ng/mL)*	4.3 (0.8)	2.34 (1.17)	1.3 (0.6)	1.15 (0.76)	0.22 (0.15)	0.55 (0.08)	0.3 (0.07)	0.44 (0.06)	1.09 (0.18)	1.76 (0.36)	1.12 (0.03)	2.49 (0.48)	1.08 (0.67)	0.46 (0.06)	0.14 (0.07)	0.41 (0.21)
Leptin *(ng/mL)*	127.4 (24.3)	195.3 (10.33)	41.3 (12.1)	171.2 (19.5)	2.28 (0.15)	2.1 (0.29)	4.64 (4.05)	2.98 (0.16)	65.05 (7.25)	130.21 (20.66)	124.8 (31.9)	113.5 (36.08)	0.68 (0.07)	0.98 (0.25)	2.23 (0.4)	0.37 (0.3)
Amylin *(ng/mL)*	1.2 (0.1)	1.33 (0.04)	0.96 (0.18)	0.9 (0.15)	1.02 (0.09)	1.30 (0.17)	0.91 (0.14)	0.74 (0.24)	0.56 (0.09)	0.71 (0.54)	0.69 (0.16)	0.28 (0.02)	0.90 (0.24)	0.48 (0.08)	1.47 (0.04)	0.015 (0.06)
Ghrelin *(ng/mL)*	0.88 (0.07)	5.8 (1.5)	0.86 (0.05)	5.4 (5.4)	0.82 (0.08)	5.28 (0.42)	0.68 (0.06)	3.36 (3.35)	0.92 (0.12)	2.76 (2.75)	0.87 (0.11)	8.48 (2.93)	0.73 (0.18)	15.58 (1.57)	0.46 (0.04)	11.99 (3.65)
CCK *(ng/mL)*	1.13 (0.03)	33.78 (11.43)	1.16 (0.07)	11.12 (0.5)	1.12 (0.06)	1.44 (0.85)	1.19 (0.06)	1.88 (0.6)	1.04 (0.05)	17.0 (0.83)	0.94 (0.06)	30.6 (12.64)	1.11 (0.01)	368.0 (3.6)	1.26 (0.07)	12.65 (7.17)
GLP-1 *(ng/mL)*	0.67 (0.07)	3.98 (1.7)	0.71 (0.11)	3.56 (0.36)	0.83 (0.11)	2.48 (0.05)	0.85 (0.10)	3.52 (1.13)	0.53 (0.03)	4.73 (1.25)	0.49 (0.05)	4.11 (0.12)	0.53 (0.04)	4.62 (0.74)	0.69 (0.1)	12.37 (2.41)
CART *(ng/mL)*	0.96 (0.1)	0.35 (0.34)	0.82 (0.1)	16.2 (0.23)	0.9 (0.13)	10.29 (7.75)	0.96 (0.12)	0.039 (0.03)	0.85 (0.1)	2.75 (2.08)	1.13 (0.17)	11.03 (6.37)	0.96 (0.14)	3.2 (2.79)	1.24 (0.08)	0.09 (0.01)
PYY *(ng/mL)*	7.79 (2.07)	21.4 (1.0)	5.47 (1.74)	28.7 (18.6)	5.94 (1.89)	126.6 (6.44)	6.41 (2.35)	289.1 (181.9)	3.87 (0.68)	3.17 (3.06)	6.0 (1.27)	14.97 (2.41)	3.70 (0.44)	81.4 (2.2)	6.99 (0.54)	739.1 (5.1)