MicroPET (µPET) Imaging in a Rat Model of Obesity and Food Restriction: Effects of food stimulation on regional brain metabolic activity

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Food intake is regulated by factors that modulate caloric requirements as well as food's reinforcing properties (Schwartz et al, 2000). Apart from genetic factors, there are others (behavioral, cultural and environmental) that play a very important role in obesity. Environmental factors include stress, food palatability & availability (particularly from energy-dense foods) (Mc-Crory et al, 1999), as well as food-related cues (Wang et al, 2004). These factors may contribute to obesity through excessive eating that may be attributed to a disruption in brain sensitivity associated with food related stimuli (Wang et al, 2004). Previously, (Wang et al, 2004) we showed that exposure to an appetitive food stimulus lead to significant activation in the human brain. In this study we examine how rodent brain metabolism responds to food presentation and how this response may depend on diet and genetic predisposition to obesity. Male Zucker Obese (fa/fa) (Ob) and Lean (Le) rats were divided into 4 groups (n=5/group): i) Ob rats with unrestricted (U) food access, ii) Ob rats with restricted (R) food access (70% of ad-lib), iii) Le U rats and iv) Le R rats. Rats were scanned using 2-[18F]-flouro-2-deoxy-D-glucose (FDG) under two conditions: without (baseline) and with a food presentation (stimulus scan). Following the baseline scan, daily presentations of a novel food (5g cooked bacon) were given for 5 days. On the 7th day, rats were scanned with the same food stimulus present. Intra-subject variability was explicitly modeled in a multifactor ANOVA, which defined all four rat groups. Regional metabolic changes corrected for brain global activity are reported (Table 1). Rats showed higher brain metabolism in cortical regions and this was consistent with our previous clinical findings (Wang et al, 2004). Also, greatest activation was seen in the hippocampus and visual system, which may indicate a direct response to a learned association of and a craving for the food stimulus presented.

Table 1. Greatest regional brain metabolic activation (baseline – challenge)

Brain Structure	Interaction Effects	F	P (uncorrected)	Stereotaxic location x, y, z (mm)
Left Hippocampus	Le R>Le U Ob R<Ob U Ob R<Le R Ob U>Le U	26.56	<0.001	-3 11 0
Right Hippocampus	Le R>Le U Ob R<Ob U Ob R<Le R Ob U>Le U	19.52	<0.001	0 12 -2
Left Somatosensory Cortex	Le R>Le U Ob R<Ob U Ob R<Le R Ob U>Le U	18.54	<0.001	2 11 -2
Left Superior Colliculus	Le R>Le U Ob R<Ob U Ob R<Le R Ob U>Le U	10.80	<0.001	-2 -9 -5
Visual Cortex	Le R>Le U Ob R<Ob U Ob R<Le R Ob U>Le U	10.29	<0.001	-3 11 4