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Title: Age- and diet-related changes of striatal dopamine D_2 receptor (D2R) binding in obese (Ob) (fa/fa) and lean (Le) Zucker rats revealed by positron emission tomography (PET) and autoradiography (ARG): part II (4-13 months)

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The importance of dopamine (DA) in obesity has been supported both by preclinical and clinical studies (Thanos, et al. 2006, Wang et al. 2001, Meguid et al. 2000, Hamdi et al. 1992). We previously showed that obese individuals have lower D2R binding availability compared to lean controls and that there is an inverse correlation between the Body Mass Index (BMI) and D2R (Wang et al. 2001). Using µPET & ARG we replicated these findings in Ob and Le Zucker rats (Thanos et al. 2006) showing that the Ob have lower D2R levels than the Le rats, as well as a distinct DA profile that responds uniquely to acute fasting under different chronic feeding regiments (Thanos et al. 2006). Age-related reduction of striatal D2R has been shown in humans (Volkow et al. 1996), primates (Morris, et al. 1999) and rats (Thanos, et al. 2006, Suzuki, et al. 2001), and we have also shown that food restriction attenuates this age-related loss of D2R from 1 to 4 months of age (Thanos, et al. 2006). In the present study we characterized differences in D2R binding between Ob and Le rats under different feeding regiments and we also assessed the influence of age (4-13 months) on striatal D2R. We used male (1 month old) Zucker Ob and Le rats, divided into the following 8 groups: 1) *Ob U & Le U* (rats fed an unrestricted amount of food), *Ob R & Le R* (rats fed 70% of the U rat diet) 2) *Ob PU & Le PU* (rats previously U (1 to 6 months) and then R (6 to 13 months), *Ob PR & Le PR* (rats previously R (1 to 6 months) and then U (6 to 13 months). Rats were scanned with µPET at 4 and 13 months of age using [^{11}C]-raclopride. Rats were then sacrificed, the brain harvested, sectioned and washed for endogenous DA and in-vitro ARG D2R binding performed using [^{3}H]-spiperone. In addition, all rats were examined for differences in body weight, daily food intake, open field locomotor activity, and blood insulin and leptin levels. These results will provide greater insight in understanding the mechanism and contribution of food restriction, DA and its receptors on obesity.

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