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Food restriction markedly increases dopamine D2 receptor (D2R) in a rat model of obesity as assessed with in-vivo muPET imaging ([11C] raclopride) and in-vitro ([3H] spiperone) autoradiography.

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Abstract

INTRODUCTION: Dopamine (DA) regulates food intake by modulating food reward and motivation but its involvement in obesity is much less understood. Recent evidence points to the involvement of leptin in the DA-related modulation of food intake. Here we assess DA D2 receptors (D2R) in a genetic rodent obesity model characterized by leptin-receptor deficiency and assess the influence of food restriction on these receptors.

METHODS: We compared D2R levels between Zucker Obese (fa/fa) and Lean (Fa/Fa) rats at 1 and 4 months of age and in two different feeding conditions (restricted and unrestricted food access) using in-vivo muPET imaging ([11C] raclopride, which is a method sensitive to competition with endogenous DA) and in-vitro ([3H] spiperone washed to ensure no competition with endogenous DA) autoradiography (ARG).

RESULTS: Both ARG and muPET showed that D2R were higher at 1 month than at 4 months of age and that food restricted animals had higher D2R than unrestricted animals. However there were significant differences in the results obtained at 4 months between ARG and muPET. ARG showed that at 1 month and at 4 months unrestricted lean rats (Le U) had significantly higher D2R binding than obese unrestricted rats (Ob U) but showed no differences between restricted obese (Ob R) and restricted lean rats (Le R). It also showed that D2R decline between 1 and 4 months of age was significantly attenuated in food restricted rats [both obese and lean]. In contrast, muPET showed that at 4 months of age, Ob U showed greater D2R availability than Le U rats but like ARG showed no differences between Ob R and Le R rats.

CONCLUSION: The lower D2R binding in Ob U than Le U rats observed with ARG most

likely reflects decreases in striatal D2 receptors levels whereas the increased availability observed with muPET is likely to reflect reduced DA release (resulting in decreased competition with endogenous DA). Lack of a significant difference between Ob R and Le R suggests that the differences in dopamine activity and D2R levels between Ob and Le Zucker rats are modulated by access to food. The ARG finding of an attenuation of the age-related loss of D2R binding corroborates previous studies of the salutary effects of food restriction in the aging process. Because [¹¹C] raclopride is sensitive to competition with endogenous DA, the higher D2R binding in obese rats with raclopride despite the lower D2R levels shown with spiperone could reflect lower extracellular DA in the Ob rats and merits further investigation.

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