

Program# 14.3
Title: Age and diet-related changes of cannabinoid 1 receptor (CB1R) binding in obese (fa/fa) and lean Zucker rats
Location: Georgia World Congress Center: Room C301
Presentation Start/End Time: Saturday, Oct 14, 2006, 1:30 PM - 1:45 PM
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The Cb1R is one of two known receptors in the endocannabinoid (EC) system associated with the intake of food. The selective Cb1R agonist WIN 55,212-2 has been shown to lead to increased adiposity and food intake (Lichtman and Cravatt 2005). The Zucker rat is a rodent model that is characterized by increased adiposity, hyperphagia, hyperinsulinemia, and hyperleptinemia (Chen and Wang, 2005) and blocking the Cb1R has been shown to reduce food intake in Zucker rats, while allowing the binding of Cb1R has been shown to increase food intake (Vickers, et al. 2003). Furthermore, obese mice treated with Cb1R antagonists gained less weight as compared to age-matched untreated animals fed a standard diet, and showed lower levels of insulin, glucose and leptin, (Poirier, et al. 2005) which are all factors related to adiposity (Mueller, et al. 1998). Moreover, mice lacking the Cb1R are resistant to diet induced obesity and show lower food intake as well as a diminished response to rewarding stimuli than controls (Sanchis-Segura, et al. 2004). The objective of this study was to understand the developmental and diet effects on brain Cb1R binding levels in a rodent model of obesity. We used male young (4 week old) Obese (Ob) and Lean (Le) Zucker rats, divided into unrestricted (U) and restricted (R) (fed 70% of unrestricted rats) diet groups. Body weight, food intake and locomotor activity were monitored throughout the duration of the experiment. Rats were sacrificed at either 1 or 4 months of age and the brains were sectioned and incubated in [³H]WIN 55,212-2 for Cb1R binding by in-vitro digital autoradiography using a high sensitivity β -Imager. Since it has been previously demonstrated that the Cb1R plays an important role in food consumption in the obese Zucker rat model, we aim to examine if there is a localized effect on Cb1R levels in specific brain regions and investigate how this is related to food consumption, craving and reward.

Disclosures: **R.C. Ramalhete**, None; **M. Michaelides**, None; **Y.K. Piyis**, None; **G. Wang**, None; **N.D. Volkow**, None; **P.K. Thanos**, None.

Support: NIDA, NIDA
NIAAA Intramural Research Program, LNI, NIAAA Intramural Research Program, LNI
U.S DOE DEAC02-98CH10886, U.S DOE DEAC02-98CH10886

[Authors]. [Abstract Title]. Program No. XXX.XX. 2006 Neuroscience Meeting Planner. Atlanta, GA: Society for Neuroscience, 2006. Online.

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