Program#/Poster#: 21.1

Title: Characterization of dopamine D_2 receptor (D2R) expression in mice lacking the dopamine D_4 receptor (D4R) using positron emission tomography (PET) and autoradiography (ARG)

Location: Georgia World Congress Center: Room B401

Presentation Start/End Time: Saturday, Oct 14, 2006, 1:00 PM - 1:15 PM

Authors: **M. MICHAELIDES[1]**, Y. K. PIYIS[1], N. LONDONO[1], K. SUCHLAND[2], M. RUBINSTEIN[3], D. K. GRANDY[2], G. WANG[1], N. D. VOLKOW[1,4], P. K. THANOS[1,4,5,6];
[1]Behavioral Neuropharmacology and Neuroimaging Lab, Brookhaven National Laboratory, Upton, NY, [2]Physiology and Pharmacology, Oregon Health Science University, Portland, OR, [3]Biology, Univ. de Buenos Aires, Buenos Aires, ARGENTINA, [4]Laboratory of Neuroimaging, NIAAA, NIH, Department of Health and Human Services, Bethesda, MD, [5]Psychology, SUNY Stony Brook, Stony Brook, NY, [6]Neuroscience, SUNY Stony Brook, Stony Brook, NY.

The D4R is a member of the D2-like receptor family, which also includes the D2R and D3R (Gan et al. 2004). D2-like receptors share similar molecular and pharmacological profiles, but they differ greatly in quantity and neuroanatomical distribution (Baldessarini and Tarazi, 1996; Neve and Neve, 1997). In humans, D4R polymorphisms have been associated with disorders such as drug abuse, pathological gambling, schizophrenia, ADHD (Gan et al. 2004; Viggiano et al. 2003) and genetic studies imply that 2 % of the population has a null allele for the D4R (Viggiano et al. 2003). There have been many studies that have assessed extensive behavioral reports of D4R mutant mice but very few have focused on the effects of D4R depletion on concentrations of other dopamine (DA) receptors (Gan et al. 2004). One study used in-vitro ARG to demonstrate that mice lacking the D4R show enhanced expression of D1R and NMDA receptors, but they did not differ in [^{3}H]nemonapride D2R binding as compared to wild-type littermates (Gan et al. 2004). In this study, we measured D2R binding using [^{11}C]raclopride μPET imaging and [^{3}H]spiperone ARG. 18 male D4R knockout (-/-), heterozygous (+/-) & wild-type (+/+) mice were scanned with μPET using [^{11}C]raclopride. Afterwards, the brain was harvested, sectioned and washed for endogenous DA and ARG D2R binding was performed using [^{3}H]-spiperone. [^{3}H]spiperone has been shown to label different receptor sites as well as different forms (short vs. long) of the D2R compared to [^{3}H]nemonapride (Vivo et al. 2006; Vile et al. 1995). Furthermore, digital ARG using a β-Imager has been shown to be 500 times more sensitive than film ARG (Langlois et al. 2005). Since ARG is a measure of receptor quantification while μPET measures the in-vivo competition of [^{11}C]raclopride and endogenous DA, using the combination of μPET and ARG will help increase our understanding of the effects of manipulating D4R genotype on D2R binding levels.

Disclosures: **M. Michaelides**, None; **Y.K. Piyis**, None; **N. Londono**, None; **K. Suchland**, None; **M. Rubinstein**, None; **D.K. Grandy**, 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. Department of Energy under contract DEAC02-98CH10886, U.S. Department of Energy under contract DEAC02-98CH10886

http://www.bnl.gov/thanoslab, http://www.bnl.gov/thanoslab

Neuroscience Meeting Planner. Atlanta, GA: Society for Neuroscience, 2006.Copyright by the Society for Neuroscience all rights reserved