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Title: Assessment of the effect of two novel and highly selective dopamine D3 receptor (D3R) antagonists (SB-277011A & NGB-2904) on food intake in a rodent model of obesity
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Authors: ***C. W. HO**¹, A. H. NEWMAN², C. R. ASHBY JR.³, M. MICHAELIDES¹, E. L. GARDNER⁴, C. A. HEIDBREDER⁵, N. D. VOLKOW^{1,6}, P. K. THANOS^{1,6,7,8};
¹Behavioral Neuropharmacology & Neuroimaging Lab, Brookhaven National Laboratory, Upton, NY, ²Medicinal Chemistry Section, NIDA Intramural Research Program, NIH, Baltimore, MD, ³Pharmaceutical Sciences, St. John's University, Jamaica, NY, ⁴Neuropsychopharmacology Section, NIDA Intramural Research Program, NIH, Baltimore, MD, ⁵Center for Drug Discovery in Psychiatry, GlaxoSmithKline Pharmaceuticals, Verona, ITALY, ⁶Laboratory of Neuroimaging, NIAAA, Department of Health and Human Services, NIH, Bethesda, MD, ⁷Psychology, SUNY Stony Brook, Stony Brook, NY, ⁸Neuroscience, SUNY Stony Brook, Bethesda, MD.

Selective blockade of the D3R with SB-277011A and NGB-2904 has been shown to inhibit cocaine cue-induced reinstatement of drug-seeking behavior (Heidbreder et al. 2005). Six week old male obese (Ob) and lean (Le) Zucker rats were maintained under a restricted feeding regiment (70 % of ad-lib). All rats were trained to lever press for a food reinforcer (45 mg pellet) under a 2 hour daily FR1 schedule. They were then subjected to vehicle treatments (i.p: saline) until <20% variation in the lever response for 3 consecutive days was achieved. Animals were then subjected to (Expt 1) increasing doses of SB-277011A (i.p: 3, 10, and 30 mg/kg) and (Expt. 2) NGB-2904 (i.p: 0.3, 1 and 3 mg/kg) for 3 days with each dose. Both experiments ended with a 3-day post-injection (PIC) period. Food (rodent chow) was supplemented if the animals did not consume the daily food allotment amount during the experiment. **Expt. 1 - SB-277011A:** A 2 way ANOVA (strain and treatment) revealed a significant decrease in food intake (g) for rats treated with SB-277011A (p<0.001). Multiple pair-wise comparison tests revealed significant differences (p<0.05) for both Ob (10 & 30 mg/kg) and Le rats (30 mg/kg) when compared to vehicle and PIC. In Ob rats there was also a significant dose dependent decrease in food intake between the 10 and 30 mg/kg doses. **Expt. 2 - NGB-2904:** A 2 way ANOVA revealed no significant differences in food intake (g) for strain and treatment. The results of these experiments will be discussed in terms of the involvement of the D3R on the CNS mechanism of obesity. In addition we will discuss, correlate and compare the present results with previous findings of these two compounds on drugs of abuse, their pharmacokinetic profile and their penetration into the brain.

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