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ORIGINAL INVESTIGATION

Cannabinoid CB1 antagonists and dopamine antagonists produce different effects on a task involving response allocation and effort-related choice in food-seeking behavior

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Abstract
Rationale Cannabinoid CB1 antagonists/inverse agonists suppress food-motivated behaviors and are being evaluated as potential appetite suppressants. It has been suggested that the effects of CB1 antagonism on food motivation could be related to actions on mesolimbic dopamine (DA). If this were true, then the effects of interference with cannabinoid CB1 transmission should closely resemble the effects of interference with DA transmission.
Objective To directly compare the effects of DA antagonists with those of CB1 antagonists/inverse agonists, the present studies employed a concurrent lever-pressing/chow-intake procedure. With this task, interference with DA transmission shifts choice behavior such that lever pressing for a preferred food is decreased but chow intake is increased.
Results Rats treated with IP injections of the DA D1 antagonist SCH39166 (ecopipam; 0.05–0.2 mg/kg) or the D2 antagonist eticlopride (0.025–0.1 mg/kg) showed substantial decreases in lever pressing and concomitant increases in chow consumption. In contrast, IP administration of the CB1 neutral antagonist AM4113 (4.0–16.0 mg/kg) or the CB1 antagonist/inverse agonist AM251 (2.0–8.0 mg/kg) decreased operant responding for pellets, but there was no corresponding increase in chow intake.
Conclusions These effects of CB1 antagonists/inverse agonists were similar to those produced by the appetite suppressant fenfluramine and by prefeeding. In contrast, low doses of DA antagonists leave primary food motivation intact, but shift behaviors toward food reinforcers that can be obtained with lower response costs. These results suggest that the effects of interference with CB1 transmission are readily distinguishable from those of reduced DA transmission.

Keywords Operant · Instrumental · Behavior · Reinforcement · Motivation · Dopamine · Behavioral economics · Reward

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Introduction

Several lines of evidence indicate that cannabinoid systems influence feeding and food-motivated behaviors. CB1 agonists have been shown to elevate levels of food intake (Jamshidi and Taylor 2001; Kirkham et al. 2002; Williams and Kirkham 1999). Moreover, food intake is impaired by CB1 receptor inverse agonists such as rimonabant (SR141716A), AM251, and AM1387 (Arnone et al. 1997; Colombo et al. 1998; Simiand et al. 1998; Williams and Kirkham 1999; McLaughlin et al. 2003, 2005, 2006; Pi-Sunyer et al. 2006; Salamone et al. 2007a), as well as by neutral CB1 antagonists including AM4113 and O-2050 (Gardner and Mallet 2006; Salamone et al. 2007a; Sink et al. 2007). Drugs that interfere with CB1 receptor transmission also have been shown to impair food-reinforced behavior (Freedland et al. 2000; McLaughlin et al. 2003, 2006; Ward and Dykstra 2005; Salamone et al. 2007a; Sink