fect from a 10-fold to a 1000-fold increase in sensitivity to naltrexone, thus approaching the sensitivity of chronically dependent animals. The presence of a stimulus to which rate suppression became conditioned was implicated. In short, both tolerance and dependence are multi-faceted processes which can be differentially modified. Experimental measurement of qualitatively different effects with quantitatively different sensitivities confounds interpretation. Until the underlying mechanisms are more clearly elucidated, conclusions regarding the dissociation of tolerance and dependence must be carefully evaluated with regard to the considerations discussed.

INVITED ADDRESS
Chair: *Sharon M. Hall*, Psychiatry Service, Veterans Administration Medical Center, San Francisco, CA.

ISSUES IN THE PREVENTION OF WEIGHT GAIN AFTER SMOKING CESSATION. Kenneth A. Perkins, Western Psychiatric Institute and Clinic, University of Pittsburgh, Pittsburgh, PA.

Weight gain following smoking cessation may inhibit attempts to quit smoking and promote relapse if an attempt is made, especially in women. Most of this weight gain appears to be due to increased eating, particularly between-meal snacking. Because of smokers' concern over this weight gain, combining weight control efforts with smoking cessation has received much attention under the assumption that preventing weight gain will enhance ex-smokers' chances of maintaining abstinence. Despite its widespread acceptance, there is essentially no direct support for this assumption. First, prospective studies have not reported that weight gain after cessation directly predicts relapse. Second, behavioral interventions to prevent this weight gain have proven to be ineffective. Pharmacological interventions, which are effective during brief periods of active use, have not been studied beyond several months' duration of treatment. Third, and most importantly, attempting to prevent weight gain after cessation may not improve long-term abstinence. In fact, results of some recent interventions indicate that adjunct weight control treatment may actually *impede* abstinence. Although contrary to common belief, these findings are very consistent with a large body of basic animal research, as well as some human studies, showing that food or weight restriction increases drug intake. It is not clear whether this effect is specific to weight reduction per se, food deprivation, or possibly reinforcement deprivation. Some evidence suggests the converse may also be true, that weight gain (or increased access to palatable food) decreases the reinforcing value of drugs and thus their intake. Therefore, rather than developing intensive strategies for combating weight gain after cessation, a more prudent and fruitful approach for basic and clinical research may be to reexamine the fundamental relationships among smoking, eating, body weight, and perhaps weight-related attitudes. If subsequent research concludes that cessation-induced weight gain is not positively related to risk of smoking relapse in weight-concerned smokers, it may be necessary to consider developing treatments designed to help these individuals accept, rather than fight, weight gain after cessation. Such a strategy may be especially warranted because of the trivial health effects of the typically modest weight gains observed after cessation.

INVITED ADDRESS
Chair: *Lewis S. Seiden*, University of Chicago, Chicago, IL.

ANTISENSE STRATEGIES FOR MODULATING DOPAMINERGIC BEHAVIOR. Benjamin Weiss, Long-Wu Zhou and Sui-Po Zhang. Medical College of Pennsylvania, Philadelphia, PA.

The behavioral and molecular effects of oligodeoxynucleotides antisense to the mRNAs encoding the various dopamine receptor subtypes were examined *in vivo* in mice. The antisense oligodeoxynucleotides were administered intraventricularly to normal mice and to mice with unilateral 6-hydroxydopamine lesions of the corpus striatum. The mice were then challenged with acute injections of dopamine agonists that cause specific behaviors in these animals. The levels of D_1 and D_2 dopamine receptor mRNA were determined by *in situ* hybridization histochemistry, and the levels of D_1 and D_2 dopamine receptors were determined by receptor autoradiography.

In normal mice administering the D_1 antisense produced a cataleptic effect and inhibited grooming behavior induced by the D_1 dopamine receptor agonist SKF 38393 but failed to block the stereotypic effects induced by the D_2 dopamine agonist quinpirole. In 6-hydroxydopamine-lesioned mice, the D_1 antisense blocked rotational behavior induced by SKF 38393, but had little or no inhibitory effects on rotations induced by quinpirole or by the muscarinic cholinergic agonist oxotremorine. Similarly, intraventricular injections of D_2 antisense blocked quinpirole-induced rotations but failed to inhibit rotations of induced by SKF 38393 or oxotremorine.

Continuous intraventricular infusion of D_1 antisense reduced the levels of D_1 dopamine receptors in corpus striatum and nucleus accumbens. Repeated treatment with D_2 antisense significantly reduced the levels of D_2 dopamine receptors and D_2 dopamine receptor mRNA in the striatum. By contrast, D_2 antisense treatment failed to alter D_1 dopamine receptors or D_1 dopamine receptor mRNA in striatum.

These results, showing that *in vivo* administration of dopamine receptor antisense oligodeoxynucleotides selectively blocks specific dopamine receptor-mediated behavior and specifically reduces the levels of the receptors and transcripts encoding the various dopamine receptor subtypes, suggest that the administration of other antisense oligodeoxynucleotides directed at the different dopamine receptor mRNAs may prove useful for uncovering the function of the other subtypes of dopamine receptors. They suggest further that antisense oligodeoxynucleotides targeted toward the transcripts for receptors and receptor subtypes for other neurotransmitters may aid in uncovering their function as well. (Supported by NIMH grant MH 42148).

INVITED ADDRESS
Chair: *James H. Woods*, University of Michigan, Ann Arbor, MI.

BEHAVIORAL INDICES OF DRUG-RECEPTOR INTERACTIONS. Charles P. France, Louisiana State University Medical Center, New Orleans, LA.

Much of behavioral pharmacology, by virtue of its descriptive approach to drug effects, lacks a strong theoretical frame-