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Lobeline antagonizes the discriminative stimulus properties of cocaine

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Lobeline has high affinity for nicotinic acetylcholine receptors and inhibits the function of vesicular and plasmalemmal monoamine transporters. Moreover, lobeline has been shown to alter the neurochemical and behavioral effects of psychostimulants. In drug discrimination studies, lobeline generalized to cocaine and diminished the stimulus properties of methamphetamine. The present study determined the effect of lobeline, nicotine, mecamylamine and hexamethonium on the discriminative stimulus properties of low doses of cocaine (1.6 or 5.0 mg/kg) or d-amphetamine (0.3 mg/kg) in rats, using a standard two-lever drug discrimination procedure for food reinforcement. Nicotine partially generalized to amphetamine and fully generalized to cocaine, although the discriminative stimulus properties of cocaine and amphetamine were not altered by mecamylamine or hexamethonium. In contrast, lobeline fully generalized to cocaine, but did not generalize to amphetamine. In antagonism tests, lobeline doses that did not generalize to cocaine decreased responding on the cocaine-paired levers. Surprisingly, lobeline did not alter the discriminative stimulus properties of amphetamine. This research further supports the supposition that nicotine, cocaine and amphetamine produce similar, but distinct subjective states. Furthermore, the present findings suggest that lobeline has a complex mechanism of action to disrupt the behavioral effects of drugs of abuse.