

EFFECT OF SA 4503 ON THE LOCOMOTOR STIMULATORY AND DISCRIMINATIVE STIMULUS PROPERTIES OF PSYCHOSTIMULANTS

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ABSTRACT

Methamphetamine and cocaine exhibit affinity (K_i value ≈ 2.2 and $2.0 \mu\text{M}$, respectively) for σ_1 sigma receptors. Sigma receptors mediate the neurotoxic properties of methamphetamine, and the convulsive and lethal effects of cocaine. However, much less is known about the interaction of sigma receptors and the behavioral properties of these psychostimulants. The development of novel, selective sigma receptor ligands have been invaluable to elucidate the interaction of these receptors with methamphetamine's behavioral properties. SA 4503 exhibits high, preferential affinity for σ_1 sigma receptors. The present study investigated the effect of SA 4503 on the locomotor stimulatory properties of methamphetamine, and discriminative stimulus properties of methamphetamine and cocaine. In the locomotor activity study, SA 4503 dose-dependently potentiated and attenuated methamphetamine-induced hyperactivity. In the drug discrimination study, SA 4503 pretreatment augmented the effect of methamphetamine to substitute for the methamphetamine and cocaine discriminative stimuli. Our findings suggest sigma receptors mediate the locomotor stimulatory properties, and the discriminative stimulus properties of methamphetamine and cocaine. Together, these observations indicate that while SA 4503 may not be a particularly effective pharmacotherapy, sigma receptors may be important targets for investigating the mechanism underlying methamphetamine- and cocaine-induced behaviors.