

*5-HT_{1A} Agonists,
5-HT₃ Antagonists
and Benzodiazepines
Their Comparative
Behavioural Pharmacology*



*Edited by
R.J. Rodgers and S.J. Cooper*



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Five Ht 1a Agonists 5 Ht 3 Antagonists And Benzodiazepines Their Comparative Behavioral Pharmacology

Rose Arny



Five Ht 1a Agonists 5 Ht 3 Antagonists And Benzodiazepines Their Comparative Behavioral Pharmacology:

5-HT1A Agonists, 5-HT3 Antagonists and Benzodiazepines R. J. Rodgers, S. J. Cooper, 1991 Topics covered in this volume include benzodiazepine receptors and their ligands effects of benzodiazepines and 5 HT 1A agonists on learning and memory and physiological and pharmacological implications of specific effects of 5 HT 1A agonists on rat sexual behaviour

Current Catalog National Library of Medicine (U.S.), 1992 First multi year cumulation covers six years 1965 70

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5-Hydroxytryptamine-3 Receptor Antagonists Francis D. King, Brian J. Jones, Gareth J. Sanger, 1993-10-22 5 Hydroxytryptamine 3 Receptor Antagonists provides a comprehensive authoritative review of the topic featuring contributions by recognized leaders in the field The book s three sections cover compound discovery and activity rationalization the use of compounds for studying 5 HT3 receptors and their applications to therapeutics This book will be an important reference for oncologists researchers working with the CNS and gastrointestinal disorders and anyone working in the 5 HT field within the pharmaceutical arena academia and medical practice 5-HT Agonists as Psychoactive Drugs Richard H. Rech, Gary A. Gudelsky, 1988 **Comparative Pharmacology of High Affinity 5-hydroxytryptamine 1A (5-HT1A) Receptor Binding Sites in Bovine Dorsal Raphe and Hippocampal Homogenates** Lawrence Gerald

Iben, 1991 **The 5-HT(1A) Receptor and Hallucinogens** Chad Jason Reissig, 2007 Use of hallucinogens such as lysergic acid diethylamide LSD continues to be a societal problem and accordingly is a major interest of the National Institute on Drug Abuse Hallucinogens are worthy of study not only because they have significant abuse liability but also because a detailed understanding of their mechanisms of action may be informative with respect to a variety of psychiatric disorders including psychosis The psychotropic actions of indoleamine e g LSD and phenethylamine e g mescaline hallucinogens appear to involve activation of 5 HT 2A receptors However this activation is modulated by other serotonergic and non serotonergic receptors The objective of the project was to determine the modulatory influence of 5 HT 1A receptors on the

stimulus effects of LSD and to determine the mechanism by which this modulation occurs It has been suggested that the 5 HT 1A receptor plays a significant modulatory role in the stimulus effects of the hallucinogen lysergic acid diethylamide LSD Initial studies sought to characterize the effects of several compounds with known affinity for the 5 HT 1A receptor on the discriminative stimulus effects of LSD Rats were trained in a two lever fixed ratio10 food reinforced task with LSD 0.1 mg/kg IP 15 min pretreatment as a discriminative stimulus Combination and substitution tests with the 5 HT 1A agonists 8-hydroxy-2-di-N-propylamino tetralin 8-OH DPAT buspirone gepirone and ipsapirone with LSD induced stimulus control were then performed The effects of these 5 HT 1A ligands were also tested in the presence of the selective 5 HT 1A receptor antagonist WAY 100 635 0.3 mg/kg SC 30 min pretreatment In combination tests stimulus control by LSD was increased by all 5 HT 1A receptor ligands with agonist properties Similarly in tests of antagonism the increase in drug-appropriate responding caused by stimulation of the 5 HT 1A receptor was abolished by administration of WAY 100 635 These data support the hypothesis that the 5 HT 1A receptor has a significant modulatory role in the stimulus effects of LSD Observations from the preceding study resulted in investigations to test the hypothesis that ligands which were active at 5 HT 2A receptors had a modulatory influence on 5 HT 1A receptor function Initial studies sought to characterize the effects of the selective 5 HT 2A antagonist M100907 on the discriminative stimulus effects of 8-OHDPAT Rats were trained in a two lever fixed ratio10 food reinforced task with the prototypical 5 HT 1A agonist 8-OH DPAT 0.2 mg/kg IP 15 min pretreatment as a discriminative stimulus Stimulus control by 8-OH DPAT was attenuated by the selective 5 HT 2A antagonist M100907 0.1 mg/kg 30 min pretreatment time In addition 8-OH DPAT generalized to the 5 HT 1A agonist buspirone 1.0 mg/kg 15 min pretreatment time and this substitution was also attenuated by M100907 These data suggest that 5 HT 2A receptors may have a role in the stimulus properties of 8-OH DPAT and that the interactions between 5 HT 1A and 5 HT 2A receptors are bidirectional in drug discrimination studies Based on our behavioral studies the mechanisms of action of LSD and the observed 5 HT 1A 5 HT 2A receptor interactions were investigated While previous studies have suggested a prominent role for 5 HT 1A and 5 HT 2A receptors in the mechanism of action of LSD glial cells and other cytological sites of action may contribute to the drug's effects To this end c-Fos was employed as a marker of cellular activation to determine the specific cell types which are activated by administration of LSD Adult male F344 rats were injected with LSD and sacrificed 90 min later Brains were removed and the prefrontal cortex was examined for c-Fos expression by immunohistochemistry Dose response studies revealed that LSD induced c-Fos expression is dose related Double labeled immunohistochemistry revealed that LSD induced c-Fos expression occurs in neurons and oligodendrocytes Because c-Fos is an inducible transcription factor these results suggest that dose related changes in gene expression may result from and contribute to the behavioral effects of LSD Our finding that LSD induced c-Fos expression occurs in oligodendrocytes suggests these cells may be involved in the acute behavioral effects of LSD or stimulated as a consequence of LSD administration

Central and Peripheral 5-HT3

Receptors Michel Hamon, 1992 Among the neurotransmitters serotonin is undoubtedly the biogenic amine that gave rise to the greatest effort in pharmacological research over the last ten years. The 5-HT₃ class of serotonin receptors occupies a privileged position as selective antagonists acting at this receptor are potential anxiolytics and antipsychotics in addition to being useful as anti-nausea and anti-emetic agents for cancer patients undergoing chemotherapy. Within this volume the best specialists in the field summarize the biochemical, pharmacological, electrophysiological and functional properties of 5-HT₃ receptors together with the potential use of 5-HT₃ ligands in the treatment of visceral dysfunctions, schizophrenia, anxiety and pain.

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